World Congress of CUTANEOUS LYMPHOMAS

OCTOBER 26-28, 2016 Alfred Lerner Hall, COLUMBIA UNIVERSITY New York, New York, USA

CHAIRS: MAARTEN VERMEER & LARISA GESKIN

SCIENTIFIC PROGRAM

<u>a</u>

Columbia University

College of Physicians and Surgeons



COLUMBIA UNIVERSITY MEDICAL CENTER Herbert Irving Comprehensive Cancer Center



International Society for Cutaneous Lymphomas

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Contacts

3RD WORLD CONGRESS OF CUTANEOUS LYMPHOMAS October 26-28, 2016 | COLUMBIA UNIVERSITY | New York, NY USA

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Columbia University College of Physicians & Surgeons 630 West 168th Street, Unit 39 | New York, NY 10032 Telephone: (212) 305-3334l Fax: (212) 305-5740 cme@columbia.edu | www.columbiacme.org

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Christina Patrone

Table of Contents

		PAGE
Conta	acts	2
Welco	ome Addresses	
\diamond	Chairs & ISCL	4
\diamond	EORTC CLTF	5
\diamond	USCLC	5
Facult	ty	6-7
CME	Information	8
Ackno	owledgements	9
Disclo	osures	10-13
Gene	ral Information	14-15
Maps		
\$	NYC Subway	16
\diamond	Columbia Campus	17
\diamond	Alfred Lerner Hall	18-19
Scient	tific Program	
\diamond	At A Glance	20
\diamond	Wednesday, October 26, 2016	21-23
\diamond	Thursday, October 27, 2016	24-27
\diamond	Friday, October 28, 2016	28-30
Poste	rs	31-33
Abstra	acts	
\diamond	Scientific Session A: Classification & Clinical Pathology	34-36
\diamond	Scientific Session B: Pathogenesis & Apoptosis	37-40
\diamond	Scientific Session C: Multinational Collaborative Studies	41-43
\diamond	Scientific Session D: Epidemiology & Population Studies	44-46
\diamond	Scientific Session E: Immunology & Immunopathogenesis	47-52
\diamond	Scientific Session F: Biomarkers	53-57
\diamond	Scientific Session G: Genetics	58-62
\diamond	Scientific Session H: Cutaneous B-cell Lymphomas	63-67
\diamond	Scientific Session I: Rare Cutaneous Lymphomas	68-71
\diamond	Scientific Session J: Quality of Life & Outcomes Studies	72-75
\diamond	Scientific Session K: Clinical Aspects	76-80
\diamond	Scientific Session L: Applied Research	81-83
\diamond	Scientific Session M: Therapeutics 1: Translational/Preclinical Studies	84-89
\diamond	Scientific Session N: Therapeutics 2: Advanced Therapies, incl. HSC Transplantation	90-95
\diamond	Scientific Session O: Therapeutics 3: Endpoints & Clinical Trials	96-101
\diamond	Scientific Session P: Clinical Management & Challenging Cases	102-109
Autho	or Index	110-120

Welcome Address



Maarten H. Vermeer, MD, PhD President, ISCL Co-chair, 3WCCL



Larisa J. Geskin, MD, FAAD Treasurer, ISCL Co-chair, 3WCCL

Dear Friends and Colleagues,

On behalf of International Society for Cutaneous Lymphomas (ISCL), we would like to welcome you to the Third World Congress of Cutaneous Lymphomas (3WCCL) at Columbia University in The City of New York on October 26-28, 2016. Following the immensely successful 1st and 2nd World Congress of Cutaneous Lymphomas in Chicago in 2010 and in Berlin in 2013, the 3WCCL is emerging to be the biggest and the most extensive meeting in the field of cutaneous lymphomas thus far with over 400 participants, 160 abstracts and over 100 oral presentations.

The 3WCCL is a collaborative effort of the ISCL, the United States Cutaneous Lymphoma Consortium (USCLC), the European Organization for Research and Treatment of Cancer Cutaneous Lymphoma Task Force (EORTC-CLTF) and Columbia University Medical Center (CUMC). The 3WCCL **Organizing Committee** reflects the global scale of this meeting with members from North and South Americas, Europe, Middle East, Australia and Asia. The diversity of the participants, including dermatologists, oncologists, radiation oncologists, pathologists and dermatopathologists, basic scientists, dermatology nurses, psychologists, pharmacologists, computational biologists, and many others, provides the most comprehensive forum for in-depth discussions covering all aspects of cutaneous lymphomas. The discussion will include the new 2016 WHO classification of lymphomas, genome-wide studies on genetic alterations in different clinical entities, the clinical implications of these molecular events on the pathogenesis of cutaneous lymphomas and their potential role as future therapy targets.

ISCL was brought to life in 1992 by a small group of cutaneous lymphoma enthusiasts, who founded ISCL in a little café in downtown New York City. The ISCL founders had a dream of organizing an umbrella organization to facilitate sharing of information to coordinate scientific activities worldwide. Since 1992, annual ISCL meetings were held across the globe, including Sydney, Australia; Cologne, Germany; Paris, France; Buenos Aires, Argentina; Kyoto, Japan and many cities in the United States. It is symbolic that nearly a quarter century later, ISCL returns to New York to have its largest meeting to date. ISCL-led efforts have improved communication and understanding of the pathological processes in cutaneous lymphomas, including quantification of the skin tumor burden in cutaneous T cell lymphoma (CTCL), a consensus report on terminology and hematologic criteria for erythrodermic CTCL, a scoring system for diagnosis of clinically typical mycosis fungoides, and a consensus report on staging and classification of CTCL. The most recent and most ambitious project of ISCL focused on improving treatment and prognosis of patients with cutaneous lymphomas under "Cutaneous Lymphoma International Consortium" (CLIC). In conjunction with the CLIC patient registry, a federated biobank is being constructed that will be of immense value for future translational studies.

The 3WCCL will allow us to assess the current state of the cutaneous lymphomas and embark on new ventures, narrowing the focus of some, while expanding others, to leverage the most of our opportunities across the globe. The 3WCCL reflects the spirit of collaboration we are working toward on all levels, for the shared goal of developing a better understanding of cutaneous lymphomas in the relentless search of a cure.

We are grateful to all for making the 3WCCL a success. We are so happy to have you join us at Columbia University in New York City!

Maarten H. Vermeer, MD, PhD President, ISCL Co-chair, 3WCCL

4

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Larisa J. Geskin, MD, FAAD Treasurer, ISCL Co-chair, 3WCCL



Welcome Address

United States Cutaneous

Lymphoma Consortium

EUROPEAN ORGANISATION FOR RESEARCH AND TREATMENT OF CANCER

Dear Colleagues and Friends,

On behalf of the EORTC - Cutaneous Lymphoma Task Force it is both a privilege and great pleasure to welcome you to this 3rd World Congress on Cutaneous Lymphoma, in New York from 26th to 28th October. The rarity of primary cutaneous

lymphomas coupled with the importance of a multidisciplinary approach to patient care requires a collaboration across the disciplines of Dermatology, Oncology, Haematology, Pathology and Palliative care. It was out of the spirit to achieve a World Wide partnership that the idea of establishing a World Congress specific to cutaneous lymphoma was born; with the aims to share international developments and foster interaction between different research groups.

As the EORTC CL Taskforce we are delighted to participate in this meeting and wholeheartedly thank the organisers for including a session specifically dedicated to our group, but of course open to all the meeting attendees. We are honoured for Joan Guitart to be delivering the Neil Smith Memorial Lecture. We also include presentations from our young investigator and highlight the ongoing trials of the Group. Our lectures are inspired by the common will of working together, sharing experiences and developing collaborative trials. We are extremely grateful to Larisa Geskin and her fantastic team at Columbia University for organising such a monumental meeting. We look forward to greeting our friends from all over the world and spend unforgettable days under the shadows of the New York skyscrapers.

Cordially Yours,

Pietro Quaglino Julia Scarisbrick Maarten Vermeer

Dear Friends and Colleagues,

On behalf of the United States Cutaneous Lymphoma Consortium we welcome you to the United States for the Third World Congress of Cutaneous Lymphomas

(3WCCL) in New York City, October 26th to 28th, 2016. It is with great anticipation that we embark on three days of dialogue and deliberation about the most recent discoveries in the field of cutaneous lymphomas here on the campus of Columbia University in The City of New York.

USCLO

Since our last WCCL in Berlin, the accelerated pace of discovery in the field of cutaneous lymphomas has inspired us. Few diseases foster more engagement and collaboration of multiple disciplines. The intellectual, geographic and cultural diversity of the attendees reflects this spirit of collaboration.

No other meeting in the world holds more promise for our patients with cutaneous lymphoma than the one you are attending. Our patients and their families wait anxiously for our return hoping that the new discoveries revealed over the next few days will improve the management of their disease.

Congratulations to Co-chair Maarten Vermeer and especially to our Co-chair Larisa Geskin and her team at Columbia University for organizing such a spectacular meeting. We hope you enjoy New York City, an architectural and cultural mecca that has attracted generations of artists and intellectuals from around the world.

Most sincerely,

John A. Zic, M.D. Elise C Secretary-Treasurer Past Pr USCLC USCLC

Elise Olsen, M.D. Past President USCLC



5

Faculty

Oleg E. Akilov, M.D., Ph.D. Martine Bagot, M.D., Ph.D. Susan Bates, M.D. Emilio Berti, M.D. Lorenzo Cerroni, M.D. Reinhard Dummer, M.D. Madeleine Duvic, M.D. Tatyana Feldman, M.D. Adolfo Ferrando, M.D., Ph.D. Genet Finnegan, MHS, PA-C Francine Foss, M.D., Ph.D. Larisa Geskin, M.D. Michael Girardi, M.D. Robert Gniadecki, M.D., Ph.D. Joan Guitart, M.D. Peter W. Heald, M.D. Emmilia Hodak, M.D. Richard Hoppe, M.D. David Horowitz, M.D. Steven Horwitz, M.D. Sam Hwang, M.D. Kenneth B. Hymes, M.D. Keiji Iwatsuki, M.D., Ph.D. Jacqueline M. Junkins-Hopkins, M.D. Marshall E. Kadin, M.D. Werner Kempf, M.D. Ellen J. Kim, M.D. Youn Kim, M.D. Robert Knobler, M.D. Sergei Koralov, Ph.D. Jo-Ann M. Latkowski, M.D. Mark G. Lebwohl, M.D. Sue A. McCann, R.N. Patricia L. Myskowski, M.D. Elise A. Olsen, M.D.

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Faculty

Brigham and Women's Cancer Center, Harvard Medical School John O'Malley, M.D., Ph.D. Pablo L. Ortiz Romero, M.D., Ph.D. Facultad de Medicina, Universidad Complutense Teresa Palomero, Ph.D. Columbia University Institute for Cancer Genetics Evangelia Papadavid, M.D., Ph.D. National and Kapodistrina Athens University, Medical School Nicola Pimpinelli, M.D., Ph.D. University of Florence Medical School Lauren C. Pinter-Brown, M.D., FACP University of California, Irvine Mayo Clinic Arizona and Mayo Clinic College of Medicine Mark R. Pittelkow, M.D. Rochester General Hospital Research Institute Brian Poligone, M.D. H. Miles Prince, MBBS, MD, AFRACMA, FRACP, FRCPA, MACD Peter MacCallum Cancer Centre and University of Melbourne Ramon M. Pujol, M.D., Ph.D. Universitat Autònoma de Barcelona Pietro Quaglino, M.D. University of Torino, Italy Christiane Querfeld, M.D., Ph.D. City of Hope Cancer Center & Beckman Research Institute Alain Rook, M.D. University of Pennsylvania Perelman School of Medicine Steven T. Rosen, M.D. City of Hope José Antonio Sanches Jr., M.D., Ph.D. University of Sao Paulo Medical School Ahmed Sawas, M.D. Columbia University College of Physicians & Surgeons Julia Scarisbrick, MBChBhons, FRCP, MD University Hospital Birmingham Stefan M. Schieke, M.D. School of Medicine and Public Health, University of Wisconsin - Madison Rudolf Stadler, M.D. Johannes Wesling Medical Centre Mailman School of Public Health, Columbia University Steven D. Stellman, Ph.D., M.P.H. Makoto Sugaya, M.D. University of Tokyo Graduate School of Medicine Steven H. Swerdlow, M.D. University of Pittsburgh School of Medicine Dana Farber Cancer Institute Marianne Tawa, RN, MSN, ANP Maarten H. Vermeer, M.D., Ph.D. Leiden University Medical Center Martin A. Weinstock, M.D., Ph.D. The Warren Alpert Medical School of Brown University Wen-Kai Weng, M.D., Ph.D. Stanford University School of Medicine Sean Whittaker, M.D. Kings College London Rein Willemze, M.D. Leiden University Medical Center Henry K. Wong, M.D., Ph.D. University of Arkansas for Medical Sciences University of Wisconsin, Department of Dermatology Gary S. Wood, M.D. Jasmine M. Zain, M.D. City of Hope Cancer Center & Beckman Research Institute Chunlei Zhang, M.D., Ph.D. Peking University Third Hospital John A. Zic, M.D. Vanderbilt University School of Medicine

CME Information

PROGRAM DESCRIPTION & OBJECTIVES

Cutaneous lymphomas comprise a subset of non-Hodgkin's lymphomas with a variety of clinical and pathological presentations. Patients with cutaneous lymphomas face many challenges related to the difficulties in establishing a diagnosis in the early stages, treatment choice, psychological and physical complications, like infections and development of secondary cancers, etc. The understanding of cutaneous lymphomas has been rapidly evolving in the last few years. Clinicians and researchers have improved diagnostic techniques, the understanding of the different lymphoma subtypes, as well as developed new treatment options. However, there is still an important gap based on the lack of dialog amongst the different medical specialties dealing with these conditions. The medical specialties involved in the care of cutaneous lymphoma patients include dermatologists, hematology/oncologists, pathologists, radiation oncologists, psychologists and other medical specialties as well as epidemiologists, immunologists and basic scientists. The program committee, representing the International Society for Cutaneous Lymphomas (ISCL), the EORTC Cutaneous Lymphoma Task Force, and the United States Cutaneous Lymphoma Consortium (USCLC), recognize there is a critical need to jointly assess the state of the art in the knowledge of these conditions and to share and learn from clinicians' experiences in their clinics and labs. In order to offset this gap, the 3rd World Congress of Cutaneous Lymphomas was developed.

The incidence rate of cutaneous lymphomas has been gradually increasing over the last few decades. By some estimates and in some geographical areas in the United States, the incidence has more than tripled in the last few decades. While major strides have been witnessed in the diagnosis and treatment of these lymphomas, cutaneous lymphomas continue to be one of the most important causes of morbidity and mortality among dermatology patients. In order to improve the understanding of the disease and advance our diagnostic and treatment of these conditions, it is imperative to create a platform for clinicians and researchers to share experiences and initiate a dialog amongst experts. Among the major advances to present and discuss, we have a new WHO-EORTC classification of cutaneous lymphomas, we have new diagnostic criteria for the diagnosis of the most common subtype or mycosis fungoides and we also have numerous new treatment options including histone deacetylase inhibitors, monoclonal antibodies and allo-stem cell transplant. The 3rd World Congress of Cutaneous Lymphomas will create a dialog amongst specialties, continents and experts to assist clinicians and researchers in achieving the ultimate goal of providing hope and effective new treatment options to patients.

The conference is designed for U.S. and international dermatologists, basic scientists, epidemiologists, hematologists, immunologists, oncologists, pathologists, radiation oncologists, and psychologists. The program committee expects 400 attendees. The participation of students and post-doctoral fellows is encouraged through reduced registration fees, oral presentations, and poster sessions. The goal is to offer a comprehensive conference to present new research, share experiences, and discuss new directions or the advancement of knowledge in cutaneous lymphomas.

At the conclusion of this activity, participants will be better able to:

- 1. Identify epidemiology trends and incidence rates of cutaneous lymphomas around the world as well as recognize the new varieties included in the WHO-EORTC classification with specific geographical peculiarities.
- 2. Distinguish the different molecular events being investigated regarding the pathogenesis of cutaneous lymphomas and assess the potential role of such molecules as future therapy targets.
- 3. Utilize novel treatment strategies such as combination topical and systemic approaches as appropriate for patients who are diagnosed with distinct subtypes of cutaneous lymphomas.
- 4. Identify the most promising molecular pathways to develop new agents for therapy and drug delivery for patients with cutaneous lymphomas.
- 5. Evaluate and recommend multidisciplinary treatment plans based on both effectiveness and appropriateness for patients with cutaneous lymphomas.
- 6. Analyze results from key U.S. and international cooperative group trials attempting to define standard of care treatments for patients with cutaneous lymphomas.

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the College of Physicians and Surgeons of Columbia University and the International Society for Cutaneous Lymphomas. The College of Physicians and Surgeons of Columbia University is accredited by the ACCME to provide continuing medical education for physicians.

AMA CREDIT DESIGNATION STATEMENT

The College of Physicians and Surgeons designates this live activity for a maximum of 19.25 AMA PRA Category 1 Credits[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity. **EVALUATIONS**

You will receive an e-mail within five days to complete an on-line evaluation of this course. Please verify you e-mail address with the registration staff.

CERTIFICATES

CME credits will be issued online once you complete the course evaluation.

Acknowledgements

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9

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10

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Robert Gniadecki None Kelly C. Gomes Manfrere Research development agency scholarship Fundação de Amparo a Pesquisa do estado de São Paulo Alejandro Ariel Gru Consulting Fees & Contracted Research Seattle Genetics Emmanuella Guenova* None Joan Guitart **Consulting Fees** Celgene Corporation & Astellas Pharma US, Inc. Contracted Research TetraLogic Pharmaceuticals Corporation & Actelion Pharmaceuticals US, Inc & Soligenix, Inc Peter W. Heald **Consulting Fees** Actelion Pharmaceuticals US, Inc. Fees received for promotional services Janssen Global Services, LLC, AbbVie Inc. & Actelion Pharmaceuticals US, Inc. Emmilia Hodak None Joyce W. Hoot None **Richard Hoppe** None David Horowitz **Consulting Fees** Champion Oncology, Inc. Travel reimbursement Carl Zeiss, Inc. Steven Horwitz **Consulting Fees** Celgene Corporation, Bristol-Myers Squibb, Millennium Pharmaceuticals, Inc., Amgen Inc., Seattle Genetics & Spectrum Pharmaceuticals, Inc. Contracted Research Celgene Corporation, Millennium Pharmaceuticals, Inc., Kyowa Kirin Pharmaceutical Development, Inc., Seattle Genetics, Spectrum Pharmaceuticals, Inc. & Infinity Pharmaceuticals, Inc. Charlotte Hurabielle None Sam Hwang Receipt of Intellectual Property Rights/Patent Holder Academic: Medical College of Winsconsin

Kenneth B. Hymes

None

Keiji Iwatsuki None Neha Jariwala None Constanze Jonak None Jacqueline M. Junkins-Hopkins None Marshall E. Kadin None Werner Kempf None Michael S. Khodadoust* None Ellen J. Kim* Advisory Board Actelion Pharmaceuticals US, Inc. Site PI, Clinical Trial Actelion Pharmaceuticals US, Inc., Soligenix, Inc. & Kyowa Kirin Pharmaceutical Development, Inc. Youn H. Kim* Consulting Fees & Contracted Research Seattle Genetics, Takeda PharmaceuticalsUSA, Inc. & Millennium Pharmaceuticals, Inc. Steering Committee Takeda Pharmaceuticals USA, Inc. & Millennium Pharmaceuticals, Inc. Lanny Kirsch Salary & Ownership Interest Adaptive Biotechnologies **Robert Knobler** Contracted Research Therakos & Actelion Pharmaceuticals US, Inc. Marvyn T. Koning None Sergei B. Koralov None Frederick Lansigan **Consulting Fees** Celgene Corporation & Seattle Genetics Contracted Research Spectrum Pharmaceuticals, Inc. & Teva Pharmaceutical Industries Ltd. Support for travel related expenses **Celgene** Corporation Liliane Laroche None Jo-Ann M. Latkowski None

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Anne M.R. Schrader Salary Leiden University Medical Center Leiden, The Netherlands Anita G. Seto Salary & Ownership Interest miRagen Therapeutics, Inc. **Rudolf Stadler** None Steven Stellman None Makoto Sugaya None Steven Swerdlow None Naomi Takahashi None Marina Torrealba None Liisa Väkevä None Suzanne van Santen None **Roberta Vasconcelos** None Maarten Vermeer None Yimeng Wang None Shay Warren None Jason Weed* None Ulrike Wehkamp None Martin A. Weinstock None

Wen-Kai Weng **Consulting Fees** Forty Seven Inc. Sean Whittaker **Consulting Fees Celgene** Corporation Independent research funds Galderma Laboratories, L.P. **Rein Willemze** None Marion Wobser None Henry K. Wong **Consulting Fees** Actelion Pharmaceuticals US, Inc., Seattle Genetics & Celgene Corporation Contracted Research Actelion Pharmaceuticals US, Inc. Gary S. Wood* None **Xuesong Wu** None Jinah Yoo None Jasmine M. Zain **Consulting Fees** Celgene Corporation, Seattle Genetics, & Spectrum Pharmaceuticals, Inc. Chunlei Zhang None John Zic None Wim Zoutman None

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General Information

The 3RD WORLD CONGRESS OF CUTANEOUS LYMPHOMAS takes place at the historic Columbia University Morningside Heights Campus at 116th Street and Broadway. The meeting venue is Alfred Lerner Hall at Columbia University, at 2920 Broadway. New York, NY 10027 at 115th Street and Broadway.

ALFRED LERNER HALL

Alfred Lerner Hall was designed by deconstructivist architect Bernard Tschumi, then Dean of Columbia's Graduate School of Architecture, Planning and Preservation, and opened in 1999. The 5,600-square-foot glass facade embodies the central themes for the building: accessibility, visibility, and an open, welcoming space. The main conference activities will take place in the Roone Arledge Auditorium with additional seating in the Roone Arledge Cinema.

WELCOME RECEPTION AT LOW LIBRARY

The Welcome Reception will take place on Wednesday, October 26th, in Low Memorial Library. Seth Low, the president of the University at the end of 19th century, sought to create an academic village in a spacious setting. Charles Follen McKim of the architectural firm of McKim, Mead, and White modeled the new campus after the Athenian agora. Low Library is the architectural centerpiece of the campus. Built in the Roman classical style, it appears in the New York City Register of Historic Places. A broad flight of steps descends from Low Library to an expansive plaza, a popular gathering place. Low Library is quick walk across the main campus quad, 1 block north of Lerner Hall.



CONGRESS DINNER CRUISE

The Congress Dinner will take place aboard the Spirit of New York cruise. Complimentary shuttle buses will transport the Congress participants on Thursday, October 27th at 5:15 pm from the Congress to Chelsea Piers on the Hudson River. Participants will be able to enjoy views of NYC skyline, the Freedom Tower, Statue of Liberty, Brooklyn and Williamsburg Bridges among many other attractions from the ample windows surrounding Spirit of New York's three climate-controlled decks. Weather allowing, views can be enjoyed at the open-air observation lounge. Tickets are \$50 for registrants, \$135 for guests and can be purchased at the Congress. Guests will have the opportunity to network with colleagues and faculty, while enjoying an open bar, reception, and dinner buffet.

Boarding begins at 6:30pm, cruise returns at 9:30pm.

Spirit Cruises New York Dock location: Chelsea Piers, Pier 61, New York, New York 10011 (21st Street & 11th Ave)

General Information

HOTELS

The designated hotels are strategically located between the Columbia University Morningside Heights Campus and major New York City attractions. They are within an 8-minute walk from both the American Museum of Natural History and Central Park and within 15-minute walk from the Beacon Theater and Lincoln Center, a home to the New York Philharmonic, Jazz at Lincoln Center, the Metropolitan Opera and the New York City Ballet. The Times Square, Broadway Theaters, Columbus Circle, Museum of Modern Art, Rockefeller Center, Empire State Building and many other attractions are within easy reach.

THE LUCERNE

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Directions by Subway: walk 1 block west to 79th Street and Broadway. Take the 1 train to 116th and Broadway, walk 1 block south to Alfred Lerner Hall on 115th and Broadway. 15 min total travel time.

NYLO

2178 Broadway New York, New York 10024 1-866-391-NYLO (6956) 1-212-362-1100 **Directions by Subway:** walk

Directions by Subway: walk 2 blocks north to 79th Street and Broadway. Take the 1 train to 116th and Broadway, walk 1 block south to Alfred Lerner Hall on 115th and Broadway. 15 min total travel time.

SHUTTLE BUS SERVICE

Complimentary bus service will be provided to and from Alfred Lerner Hall at Columbia University and the Lucerne and NYLO hotels, and for those attending the Congress Dinner Cruise.

Departure at 7:00 AM from the Lucerne Hotel @ 201 West 79th Street, New York, NY 10024 and the NYLO Hotel @ 2178 Broadway New York, New York 10024 to Alfred Lerner Hall at Columbia University. Please gather in the hotel lobby, 10 minutes prior to the stated departure time, for boarding.

Buses will leave each day to return to the hotels. Buses will not be held for latecomers.

Return Schedule:

Wednesday, October 26, 2016 @ 7:30 PM to Lucerne and NYLO hotels Thursday, October 27, 2016 @ 5:15 PM from Lerner Hall to Spirit Cruises Thursday, October 27, 2016 @ 9:30 PM from Spirit Cruises to Lucerne and NYLO hotels Friday, October 28, 2016 @ 5:15 PM to Lucerne and NYLO hotels

MEALS

Breakfast and Lunch will be provided daily during the duration of the Congress, along with coffee for breaks.

WEATHER

During the month of October, the temperatures are moderate with an occasional rainfall. The average temperature for the city is 60°F (16°C), from highs of 68°F (20°C) during the daytime to lows of 51°F (12°C) after dark.

COAT CHECK Complimentary coat check will be provided at Lerner Hall and Low Library

ADDITIONAL TRAVEL INFORMATION www.nycgo.com

BROADWAY TICKET DISCOUNTS www.nytix.com/Broadway

CHILD CARE www.barnardbabysitting.com

PHOTOGRAPHY

Due to the sensitive nature of the scientific material being presented, no photography will be permitted. A professional photographer will be on site, and pictures of presenters and events will be made available online after the Congress.

Map: NYC SUBWAY



Map: COLUMBIA CAMPUS



Map: ALFRED LERNER HALL



2ND FLOOR



A ROONE ARLEDGE AUDITORIUM B POSTERS A-I C REGISTRATION

- D COAT CHECK
- E EXHIBITS

18

CATERING

G ROONE ARLEDGE CINEMA (overflow seating)
H POSTERS J-P (BROADWAY ROOM)
I RAMP LOUNGE EAST
J RAMP LOUNGE WEST
K ATM
RESTROOMS

Map: ALFRED LERNER HALL





Scientific Program AT A GLANCE

	WEDN	ESDAY	TI	HURSDA	Y	FRI	DAY
7:00	Registration &	EORTC CLTF	Registration	ISCL Board	d Meeting	Registration &	USCLC Board
	Breakfast	Board Meeting	& Breakfast			Breakfast	Meeting
8:00				F. Biomarkers	i	M. Thera	peutics 1
	Weld	come					
9:00	A. Classification	n and Pathology					
			Plenar	y Session: Gei	nomics		
10:00			Plenary	Session: Epig	enetics		
	B. Pathogenes	sis & Apoptosis		Awards			
11.00				G. Genetics		N. Thera	peutics 2
11.00							
						ISCL Gener	ral Meeting
12:00	Lui	nch	0	Lunch		Lunch	CME
	Poster Prese	ntations [A-I]		EORIC	USCLC General		Symposium
12.00	C Multination			General	Meeting		
13:00	C. Mutunationa Stu	dies		Meeting			
			H. Cutane	ous B-Cell Ly	mphomas	O. Thera	peutics 3
14:00	D. Epidemiolog	gy & Population					
	Stu	dies					
15.00			I. Rare C	utaneous Lym	phomas		
15.00	E. Immu	nology &	d				
	Immunopa	thogenesis				P. Clinical Ma	anagement &
16:00			J. Quality of	K. Clinical	L. Applied	Challeng	ing Cases
			Life &	Aspects	Research		
17.00	Poster Prese	ntations [LP]	Outcomes Shutt	le to Dinner (ruico	Conc	lusion
17.00			51141				
	Welcome Rec	ception in Low					
18:00	LID	iary	C			PLENARY/C	ME SESSIONS
			Cong	ress Dinner C	ruise	POSTER PRE	
19.00						*not CME accr	edited
20:00							
21:00							

20

WELCOME EVENTS SCIENTIFIC SESSIONS PLENARY/CME SESSIONS POSTER PRESENTATIONS* SOCIETY MEETINGS* *not CME accredited

07:00-08:30 Registration & Breakfast

Scientific Program wednesday, october 26, 2016

ALL EVENTS IN ROONE ARLEDGE AUDITORIUM UNLESS OTHERWISE NOTED

07:00-08:30 EORTC CLTF Board Meeting [Ramp Lounge West] 08:30-08:45 Welcome Remarks Maarten Vermeer & Larisa Geskin 08:45-10:10 Scientific Session A. Classification & Clinical Pathology Min Chairs: Willemze, Guitart, Kempf, Swerdlow ◊ Cutaneous Lymphomas & the 2016 WHO Classification Steven Swerdlow 20 A-01 Studies in folliculotropic MF and transformed MF: consequences for the ISCL/EORTC **Rein Willemze** 15 staging system A-02 Primary Cutaneous Aggressive Epidermatropic T-Cell Lymphomas: reappraisal of a provi-Joan Guitart 7+2 sional entity in the 2016 WHO classification of Lymphomas A-03 Primary Cutanous CD8-Positive Aggressive Epidermotropic Cytotoxic T-Cell Lymphoma: Emilio Berti 7+2 Clinico-Pathological Features and Genomic Alterations A-04 CD8+ mycosis fungoides: an indolent lymphoproliferative disorder Estela Martinez-7+2 Escala A-05 Unilesional mycosis fungoides is associated with increased expression of miR-17~92, Th1 Lilach Moyal 7+2 cytokine profile and absence of Th2 A-06 Pediatric mycosis fungoides: Clinicopathologic characteristics and outcome and a study Emmilia Hodak 7+2 of the human leukocyte antigen system 10:10-10:30 Break & Poster Viewing - generously supported by a grant from Actelion 10:30-12:00 Scientific Session B. Pathogenesis & Apoptosis Chairs: Wood, Gniadecki, Pujol, Wong B-01 Introduction + Apoptotic Abnormalities in CTCL: Pathogenetic and Therapeutic Implica-Gary Wood 13+2 tions B-02 Micro RNA regulatory circuits in chemotherapy-induced apoptosis in CTCL cells Robert Gniadecki 7+2 B-03 Investigating the role of PLCG1 mutations in Sézary Syndrome Varsha M. Patel 7+2 B-04 A comparison of transcriptome sequencing and TOX DamID sequencing data identifies Brittany O. 7+2 putative downstream effects of transcription factor dysregulation in Sézary syndrome Dulmage B-05 Inactivation of runx3/p46 Promotes Cutaneous T-Cell Lymphoma Chalid Assaf 7+2B-06 STAT3 activation results from the epigenetic abrogation of miR-124 in Cutaneous T-cell Fernando 7+2 lymphoma Gallardo B-07 Novel high-throughput virome capture sequencing technique to identify viral pathogens Mary E. Anderson 7+2 in patients with cutaneous T-cell lymphoma B-08 Mitochondrial retrograde signaling regulates sensitivity to metabolic stress and allows Stefan M. Schieke 7+2

3RD WORLD CONGRESS OF CUTANEOUS LYMPHOMAS | OCTOBER 26-28, 2016 | COLUMBIA UNIVERSITY 21

selective targeting of cutaneous T-cell lymphoma

Scientific Program wednesday, october 26, 2016

12:00-12:30	Lunch		
12:30-13:00	Poster Presentations A-I [Broadway room]		
13:00-14:00	Scientific Session C. Multinational Collaborative Studies		
	Chairs: Scarisbrick, Quaglino, Olsen, Y. Kim		
\$	Introduction	Youn H. Kim	5
C 04			0.0
C-01	Uniting International Expert Centres to Evaluate and Validate the Prognostic Index Model	Julia Scarisbrick	8+2
C-02	PROspective Cutaneous Lymphoma International Study (PROCLIPI) in Early Stage Mycosis Fungiodes	Julia Scarisbrick	8+2
C-03	Global Patterns of Care in Advanced Stage Mycosis Fungoides/Sezary Syndrome: A Multicenter Retrospective Follow-up Study from the Cutaneous Lymphoma International Consortium	Pietro Quaglino	8+2
C-04	Validation of Central Pathology Review in Advanced-Stage Cutaneous T-cell Lymphomas, a Multi-Institutional and International Pathology Pilot Study	Alejandro Ariel Gru	10+2
C-05	USCLC update	Elise Olsen	8+2
14:00-15:00	Scientific Session D. Epidemiology & Population Studies		
	Chairs: Knobler, Zhang, Weinstock, Stellman		
\$	Introduction	Martin Weinstock	10
\$	Introduction	Steven Stellman	15
D-01	Relative frequency, clinical features, and survival outcomes of 395 patients with cutaneous lymphoma in Korea: a subgroup analysis per 10-year period	Woo Jin Lee	7+2
D-02	Characterization of 794 cutaneous lymphoma patients from a single center in Brazil	Denis Miyashiro	7+2
D-03	Cutaneous T-cell Lymphoma in Saudi population	Yousef Binamer	7+2
15:00-15:20	Break & Poster Viewing - generously supported by a grant from Horizon		
15:20-17:00	Scientific Session E. Immunology & Immunopathogenesis		
	Chairs: Rook, Sugaya, Querfeld, O'Malley		
\$	Introduction	Alain Rook	10
E-01	The immune checkpoint receptors ICOS and PD1 in mycosis fungoides and Sézary syn- drome: correlation with disease and outcome.	Christiane Querfeld	7+2
E-02	Lack of support for a Th2 origin of Mycosis fungoides revealed by RNA sequencing	Nicolas Bastidas- Torres	7+2

Scientific Program wednesday, october 26, 2016

E-03	Interleukin-13 is over-expressed in cutaneous T-cell lymphoma cells and regulates their proliferation	Patrizia Fuschiotti	7+2
E-04	Dysfunctional cytokines production induced by Toll-like receptors activation in the Sézary syndrome	Kelly C. Gomes Manfrere	7+2
E-05	TIGIT and Helios are Highly Expressed on CD4 T-Cells in Sezary Syndrome	Neha Jariwala	7+2
E-06	Mycosis fungoides: new issues from microenvironment	Alessandro Pileri	7+2
E-07	Impaired Secretion of CXCL9/MIG and CXCL10/IP-10 in Sezary Syndrome	Marina Torrealba	7+2
E-08	Ineffective antibody-dependent cellular cytotoxicity in patients with late stage cutaneous T cell lymphoma	Emmanuella Guenova	7+2
E-09	Characterization of the tumor microenvironment in primary cutaneous CD30-positive lymphoproliferative disorders: a predominance of CD163-positive M2 macrophages	Werner Kempf	7+2
E-10	IL-10 is a biomarker of advanced mycosis fungoides and is required for maximal tumor formation in a murine model of CTCL	Xuesong Wu	7+2
17:00-17:30	Poster Presentations J-P [1st floor]		

17:30-19:30 Picture Taking & Welcome Reception at Low Library



ALL EVENTS IN ROONE ARLEDGE AUDITORIUM UNLESS OTHERWISE NOTED

07:00-08:00	Registration & Breakfast		
07:00-08:00	ISCL Board of Directors Meeting [Ramp Lounge West]		
08:00-09:30	Scientific Session F. Biomarkers		Min
	Chairs: Bagot, Stadler, Iwatsuki, Geskin		
\$	Introduction	Martine Bagot	10
F-01	Increased Soluble CD226 in Sera of Patients with Cutaneous T-Cell Lymphoma Mediating Cytotoxic Activity against Tumor Cells via CD155	Naomi Takahashi	7+2
F-02	Evaluation of validated DNA methylation biomarkers in early Sézary syndrome patients	Wim Zoutman	7+2
F-03	Variability in CD30 and other biomarkers in Mycosis Fungoides/Sézary Syndrome (MF/SS): Challenges in Tissue Biomarker Interpretation	Ziba Rahbar	7+2
F-04	CXCL13 and BOB1 expression in initial biopsies of mycosis fungoides with stable early stage and later tumor stage disease	Ulrike Wehkamp	7+2
F-05	Usefulness of KIR3DL2 to diagnose, follow-up and manage the treatment of Sézary syn- drome patients	Charlotte Hurabielle	7+2
F-06	c-MET is overexpressed in cutaneous T-cell lymphoma and represents a potential thera- peutic target	Chalid Assaf	7+2
F-07	Biological and clinical significance of tryptophan catalyzing enzymes in patients with cuta- neous T-cell lymphoma	Liisa Väkevä	7+2
F-08	Cell adhesion molecule 1 is a biomarker for leukemic cells in progressive or refractory Sézary syndrome	Keiji Iwatsuki	12+2
F-09	A reactivation signal, BZLF-1, is a biomarker for severe phenotypes of cutaneous EBV-as- sociated T/NK lymphoproliferative disorders	Keiji Iwatsuki	
09:30-09:50	Break & Poster Viewing - generously supported by a grant from Mallinckrodt		
09:50-10:10	Plenary Session: Genomic and Mutational Landscape in T-cell Lymphomas	Adolfo Ferrando	20
10:10-10:30	Plenary Session: Epigenetics of CTCL	Maarten Vermeer	20
10:30-10:35	Awards Ceremony		5
10:35-12:00	Scientific Session G. Genetics		
	Chairs: Whittaker, Girardi, Ortiz-Romero, Palomero		
\$	Introduction of CTCL Genomics	Teresa Palomero	10
G-01	Validation and functional interrogation of JAK and STAT variants in Primary Cutaneous T-cell Lymphoma (CTCL)	Rosie M. Butler	7+2
G-02	Direct gene expression measurement in skin helps predict long-term clinical outcome in patients with cutaneous T-cell lymphomas	Adele de Masson	7+2
G-03	Development of an in vitro CTCL platform for screening targeted molecular agents	Jason Weed	7+2

G-04	Lessons Learned From a Novel Mouse Model of CTCL	Sergei B. Koralov	7+2
G-05	High-throughput T cell receptor sequencing transforms care of cutaneous T cell lympho- ma patients	John O'Malley	7+2
G-06	TCR sequencing facilitates diagnosis and identifies mature T cells as the cell of origin in cutaneous T-cell lymphoma	Lanny Kirsch	7+2
G-07	Integrative analysis of genomic data to identify common genomic alterations in cutaneous T-cell lymphoma	Li-Wei Chang	7+2
G-08	Genomic landscape of Mycosis fungoides	Jinah Yoo	7+2
12:00-13:30	Lunch & Poster Viewing		
<mark>12:15-13:30</mark>	EORTC CLTF Group Meeting		
\$	Neil-Smith Memorial Lecture: Reflections in the diagnosis of CD30 lymphoproliferative disease	Joan Guitart	
\$	Young Investigator Presentation		
\$	Translational Research: Resminostat Maintenance Trial	Maarten Vermeer	
\$	NGS studies in cutaneous B-cell lymphomas	Kees Tensen	
\diamond	Summary EORTC Board Meeting, close		
12:30-13:30	USCLC General Meeting [Room 555]		
13:30-14:25	Scientific Session H. Cutaneous B-cell lymphomas		
	Chairs: Hodak, Junkins-Hopkins, Guitart		
\$	Introduction	Joan Guitart	10
H-01	Immunoglobulin constant region mutations in Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type	Marvyn T. Koning	12+2
H-02	The B-Cell Receptor of Primary Cutaneous Follicle Center Lymphoma: Implications for Pathogenesis	Marvyn T. Koning	
H-03	PD1 and PD-L1 expression in primary cutaneous diffuse large B cell lymphoma	Christina Mitteldorf	7+2
H-04	Primary cutaneous diffuse large B-cell lymphoma, leg-type: high frequency, diagnostic and prognostic value of MYD88 L265P mutation	Anne Pham- Ledard	7+2
H-05	Primary Cutaneous B-Cell Lymphoma – Systemic spread is rare whilst cutaneous relapses and secondary malignancies are frequent	Sue Ann Chan	7+2

14:25-14:45 Break & Poster Viewing - generously supported by a grant from Valeant

	Scientific Session I. Rare Cutaneous Lymphomas		
	Chairs: Kadin, Berti, Cerroni, Rosen		
I-01	Introduction + A new look at atopy in CD30+ Cutaneous Lymphoproliferative Disorders	Marshall Kadin	13+2
I-02	TOX expression in cutaneous T-cell lymphomas and cutaneous B-cell lymphomas	Anne M.R. Schrader	12+2
I-03	No TP63 rearrangements in a selected group of primary cutaneous CD30+ lymphoprolif- erative disorders with aggressive clinical course	Anne M.R. Schrader	
1-04	Skin manifestations and outcome in adults with pre-B cell acute lymphoblastic leukemia; an important differential diagnosis to primary cutaneous follicle center lymphoma, diffuse type and secondary cutaneous follicular lymphoma	Yann Charli- Joseph	7+2
I-05	Cutaneous manifestations of Adult T-cell lymphoma/leukemia. Monocentric study of 37 patients between 1996 and 2016.	Charlotte Hurabielle	7+2
I-06	Blastic Plasmacytoid Dendritic Cell Neoplasm: an update on cytogenetic data	Silvia Alberti- Violetti	7+2
I-07	Expression of TFH markers and detection of RHOA p.G17V and IDH2 p.R172K/S muta- tions in cutaneous localizations of angioimmunoblastic T-cell lymphomas	Nicolas Ortonne	7+2
15:50-16:00	Break		
16:00-17:00	Scientific Session J: Quality of Life & Outcomes Studies		
	Chairs: Zic, McCann, Tawa, Finnegan		
\$	Introduction	John Zic	10
J-01	Cost-Effectiveness Analysis of Systemic Treatments for Cutaneous T-Cell Lymphoma	Larisa Geskin	7+2
J-02			
	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome	Stacey McCaffrey	7+2
J-03	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome Large prospective observational registry in MF-CTCL	Stacey McCaffrey Ellen J. Kim	7+2 7+2
J-03 J-04	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome Large prospective observational registry in MF-CTCL Assessment of QOL, illness perception, and illness behavior in 92 patients with primary cutaneous lymphoma	Stacey McCaffrey Ellen J. Kim Constanze Jonak	7+2 7+2 7+2
J-03 J-04 J-05	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome Large prospective observational registry in MF-CTCL Assessment of QOL, illness perception, and illness behavior in 92 patients with primary cutaneous lymphoma Caregiver Burden and Qulaity of Life Factors Affecting Caregivers of Patients with Cutane- ous T-Cell Lymphoma	Stacey McCaffrey Ellen J. Kim Constanze Jonak Sue A. McCann	7+2 7+2 7+2 7+2
J-03 J-04 J-05 16:00-17:00	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome Large prospective observational registry in MF-CTCL Assessment of QOL, illness perception, and illness behavior in 92 patients with primary cutaneous lymphoma Caregiver Burden and Qulaity of Life Factors Affecting Caregivers of Patients with Cutane- ous T-Cell Lymphoma Scientific Session K. Clinical Aspects	Stacey McCaffrey Ellen J. Kim Constanze Jonak Sue A. McCann	7+2 7+2 7+2 7+2
J-03 J-04 J-05 16:00-17:00	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome Large prospective observational registry in MF-CTCL Assessment of QOL, illness perception, and illness behavior in 92 patients with primary cutaneous lymphoma Caregiver Burden and Qulaity of Life Factors Affecting Caregivers of Patients with Cutane- ous T-Cell Lymphoma Scientific Session K. Clinical Aspects Chairs: Pinter-Brown, Pittelkow, Sanches, Myskowski	Stacey McCaffrey Ellen J. Kim Constanze Jonak Sue A. McCann	7+2 7+2 7+2 7+2
J-03 J-04 J-05 16:00-17:00 ◊	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome Large prospective observational registry in MF-CTCL Assessment of QOL, illness perception, and illness behavior in 92 patients with primary cutaneous lymphoma Caregiver Burden and Qulaity of Life Factors Affecting Caregivers of Patients with Cutane- ous T-Cell Lymphoma Scientific Session K. Clinical Aspects <i>Chairs: Pinter-Brown, Pittelkow, Sanches, Myskowski</i> Introduction	Stacey McCaffrey Ellen J. Kim Constanze Jonak Sue A. McCann Patricia Myskowsk	7+2 7+2 7+2 7+2 i 10
J-03 J-04 J-05 16:00-17:00 ◊ K-01	Development and validation of the first measure of quality of life specific for patients with Mycosis Fungoides/Sézary syndrome Large prospective observational registry in MF-CTCL Assessment of QOL, illness perception, and illness behavior in 92 patients with primary cutaneous lymphoma Caregiver Burden and Qulaity of Life Factors Affecting Caregivers of Patients with Cutane- ous T-Cell Lymphoma Scientific Session K. Clinical Aspects <i>Chairs: Pinter-Brown, Pittelkow, Sanches, Myskowski</i> Introduction Cutaneous lymphomas during anti-tumor necrosis factor therapy are often associated with misdiagnosed "psoriasis" or poorly characterized "dermatitis"	Stacey McCaffrey Ellen J. Kim Constanze Jonak Sue A. McCann Patricia Myskowsk Estela Martinez- Escala	7+2 7+2 7+2 i 10 7+2

K-03	Sézary syndrome without erythroderma	Liliane Laroche	7+2
K-04	Risk of venous thromboembolism in patients with parapsoriasis (early mycosis fungoides): A Danish nationwide population-based cohort study	Lise M. Lindahl	7+2
K-05	Protean Manifestations of Early Sézary Syndrome	Robert Gniadecki	7+2
16:00-17:00	Scientific Session L. Applied Research		
	Chairs: Schieke, Hwang, Koralov, Gniadecki		
L-01	Introduction + An in vitro model of psoralen ultraviolet A (PUVA)-induced apoptosis of cu- taneous lymphoma cell lines: Augmentation by type I interferons via JAK1-STAT1 pathway	Robert Gniadecki	15
L-02	MYD88 mutations in a distinct type of cutaneous marginal zone lymphoma with a non- class switched IgM-immunophenotype	Marion Wobser	7+2
L-03	Analysis of the expression and activity of metalloproteinases 2 and 9 and their inhibitors and correlation with histological findings and prognosis in mycosis fungoides	Roberta Vasconcelos	7+2
L-04	Impact of immunodeficiency on outcomes and immune-checkpoint molecule expression in mycosis fungoides	Shay Warren	7+2
L-05	Role of PAK1 in the onset and progression of cutaneous T-cell lymphoma	Yimeng Wang	7+2
L-06	Doxycycline is an NF-kB Inhibitor That Induces Apoptotic Cell Death in Malignant T-cells	Brian Poligone	7+2

17:15-18:15 Shuttle to Dinner Cruise at Chelsea Piers, Pier 61, New York, New York 10011 (21st Street & 11th Ave)

18:15-21:30 Congress Dinner Cruise - generously supported by a grant from Actelion



Scientific Program FRIDAY, OCTOBER 28, 2016

ALL EVENTS IN ROONE ARLEDGE AUDITORIUM UNLESS OTHERWISE NOTED

07:00-08:00 Registration & Breakfast

07:00-	08:00	USCLC Board of Directors Meeting [Ramp Lounge West]		
08:00-	09:10	Scientific Session M. Therapeutics 1a: Translational/Pre-clinical Studies		Min
		Chairs: Zain, Papadavid, Prince, Bates		
	٥	Introduction + CTCL as a disease of epigenetic dysregulation	Susan Bates	15
	M-01	Novel treatment option for CTCL: Studying the effects of dimethylfumarate from bench to bedside	Jan P. Nicolay	7+2
	M-02	Translational Development of MRG-106, an Oligonucleotide Inhibitor of miR-155, as a Novel Therapy for CTCL	Anita G. Seto	7+2
	M-03	Chimeric Antigen Receptor Modified T cells Targeting Chemokine Receptor CCR4 as a Therapeutic Modality for T-cell Malignancies including CTCL	Marshall E. Kadin	7+2
	M-04	Differential transcriptome response in mycosis fungoides patients following silicon phtha- locyanine 4 photodynamic therapy	Sayeeda Ahsanuddin	7+2
	M-05	Preclinical Investigation of SGN-CD70A Drug-Antibody Conjugate in T Cell Lymphomas	Wei Ai	7+2
	M-06	Characterization of CD70 immunoperoxidase staining on cutaneous T-cell lymphomas	Laura B. Pincus	7+2
09:10-	09:20	Quick Break and switch Chairs		

09:20-10:30	Scientific Session M. Therapeutics 1b: Translational/Pre-clinical Studies		
	Chairs: Dummer, Whittaker, Pimpinelli, Bates		
M-07	Synergy of romidepsin and mechlorethamine in cutaneous T-cell lymphoma	Christina C. Patrone	7+2
M-08	RARa/RXR Synergism Potentiates Responsiveness in Cutaneous T Cell Lymphoma	Sebastian S. DeMarco	7+2
M-09	AN-7 sensitizes cutaneous T-cell lymphoma cell lines to doxorubicin via inhibition of double-strand break repair	Lilach Moyal	7+2
M-10	Resminostat - an epigenetic approach for CTCL maintenance treatment	Matthias Borgmann	7+2
M-11	Apoptosis induction in Cutaneous T-cell Lymphoma Cells after Treatment with Lenalido- mide	Lia Papadavid	7+2
M-12	Targeting CK1 Epsilon as a Novel Therapeutic Strategy in c-Myc Driven Lymphoma	George Deng	7+2

10:30-10:45 Break & Poster Viewing

10:45-11:45 Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation				
Chairs: Foss, Horowitz, Hoppe, Weng				
Introduction + Role of Allogeneic HSC Transplantation CTCL	Jasmine M. Zain	15		

Scientific Program FRIDAY, OCTOBER 28, 2016

N-01	Long-term outcome of allogeneic hematopoietic stem cell transplantation for patients with mycosis fungoides and Sézary syndrome	Francesco Onida	8+2
N-02	Allogeneic Stem Cell Transplantation in Refractory MF/SS: Results with Reduced Intensity Conditioning Regimen	Francine Foss	14+2
N-03	Pralatrexate in Cutaneous T cell Lymphoma: Retrospective Experience with and without Leucovorin	Francine Foss	
N-04	Low dose Total Skin Electron Beam therapy (TSEB) 12Gy in 8 # over 2 weeks. The results in 103 patients from the UK.	Stephen Lloyd Morris	8+2
N-05	The French Experience of Chlormethine Gel for the Treatment of Mycosis Fungoides:A Retrospective Series of 107 cases	Steve Mathieu	8+2
11:45-12:00	ISCL General Meeting		
12:00-13:30	Lunch & Poster Viewing		
12:00-13:30	CME SYMPOSIUM: Immunology & Immunotherapy of Cutaneous Lymphomas - gener- ously supported by grants from Actelion & Horizon		
\diamond	Animal Models as a Means to Study the Tumor Microenvironment in CTCL	Sam Hwang	15+3
\diamond	Pathogenesis of Immune Compromise in the CTCL Patient	Michael Girardi	15+3
\diamond	Importance of the Innate Immune Response in Therapy of CTCL	Alain Rook	15+3
\$	New Immunotherapies in Clinical Development	Youn H. Kim	15+3
13:30-14:35	Scientific Session O. Therapeutics 3a: Endpoints & Clinical Trials		
	Chairs: Horwitz, Bagot, Y. Kim, Lebwohl		
\$	Introduction + Landscape of new therapeutics in CL	Steven Horwitz	13+2
O-01	Exploring New Meaningful Endpoints for CTCL Clinical Trials in Two Phase II Studies of Brentuximab Vedotin (BV) in Patients with Mycosis Fungoides (MF) and Sézary Syndrome (SS)	Youn H. Kim	8+2
O-02	KIR3DL2 expression in cutaneous T-cell lymphomas: a widely-shared target	Maxime Battistella	18+2
O-05	First-in-Human, open label, multicenter phase 1 study of IPH4102, first-in-class humanized anti-KIR3DL2 mAb, in relapsed/refractory CTCL: preliminary safety and clinical activity results	Martine Bagot	8+2
O-03	E7777 Demonstrated Safety in Persistent or Recurrent Cutaneous T-Cell Lymphoma	Madeleine Duvic	8+2
O-04	A Single-arm Phase 2A Study of NM-IL-12 (rHu-IL12) in Patients with Mycosis Fungoi- des-Type CTCL (MF) Undergoing Low-Dose Total Skin Electron Beam Therapy (LD-TSEBT)	Richard Hoppe	8+2
14:35-14:45	Quick Break and switch Chairs		
14:45-15:35	Scientific Session O. Therapeutics 3b: Endpoints & Clinical Trials		

Chairs: Feldman, Duvic, Akilov, Sawas

> O-06 Lenalidomide in relapsed or refractory primary cutaneous large B-cell lymphomas, leg-Marie Beylot-Barry 8+2 type: first results of a multicentric prospective phase II trial "REV-LEG"

Scientific Program FRIDAY, OCTOBER 28, 2016

	O-07	Phase 1, Single-Arm, Open-Label, Dose Escalation Trial of Microneedle Array-Doxorubicin in Patients with Cutaneous T cell Lymphoma	Oleg Akilov	8+2
	O-08	Interim analysis of phase II clinical trial PimToMF (Topical Pimecrolimus in early MF) Eudra CT 2014-001377-14	Pablo L. Ortiz Romero	8+2
	O-09	A First in Human Experience of the Anti-CD37 Antibody-Drug Conjugate AGS67E in Lymphoid Malignancies, with Exciting Early Activity in CTCL	Ahmed Sawas	8+2
	O-10	Pembrolizumab for Treatment of Relapsed/Refractory Mycosis Fungoides and Sézary Syndrome: Clinical Efficacy in a CITN Multicenter Phase 2 Study	Michael S. Khodadoust	8+2
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15:35-15:50 Break & Poster Viewing

15:50-16:50	Scientific Session P: Clinical Management & Challenging Cases		
	Chairs: Heald, Hymes, Latkowski, E. Kim		
\$	Introduction	Peter Heald	10
P-01	The Effect of Phototherapy on Progression to Tumors in Patients with Patch-Plaque Stage Mycosis Fungoides	Joyce W. Hoot	6+2
P-02	Total Skin Electron Beam (TSEB) therapy for the management of T cell cutaneous lympho- mas. The evolving role of low dose (12 Gy) treatment schedule	John Georgakopoulos	6+2
P-03	Eyelid involvement by MF/CTCL: a management challenge	Ellen J. Kim	6+2
P-04	The French Experience of Treatment of Cutaneous T Cell Lymphoma with Brentuximab Vedotin: A series of 32 Cases	Steve Mathieu	6+2
P-05	Evaluation of treatment in indolent and aggressive subgroups of folliculotropic mycosis fungoides	Suzanne van Santen	6+2
P-06	Treatment of early-stage folliculotropic mycosis fungoides: A single-center experience	Iris Amitay-Laish	6+2

16:50-17:00 Congress Conclusion & Closing Remarks

Maarten Vermeer & Larisa Geskin



Posters

ABSTRACTS PRESENTED AS ORALS WILL ALSO BE PRESENTED AS POSTERS USING THE NUMBERS REFERENCED IN THE SCIENTIFIC PROGRAM OF EVENTS

	Scientific Session A. Classification & Clinical Pathology	Presenting Author
A-07	Psoriasis in Patients with Mycosis Fungoides: A Clinicopathologic Study of 25 patients	Vasiliki Nikolaou
	Scientific Session D. Epidemiology & Population Studies	
D-04	Primary Cutaneous Lymphoma in Argentina: Analysis of 416 Cases of the Primary Cutaneous Lymphoma Network. Cutaneous Lymphoma Argentine Group	Alejandra Abeldaño
D-05	Cutaneous Manifestations of Angioimmunoblastic T-cell lymphoma in an Asian population: Clin- ical characteristics and challenges	Mark Jean-Aan Koh
D-06	Phototherapy for the treatment of mycosis fungoides in Asian children	Mark Jean-Aan Koh
	Scientific Session E. Immunology & Immunopathogenesis	
E-11	Significance of IL-31 expression in skin and in serum in pathogenesis of CTCLs and in patho- mechanism of accompanying pruritus	Berenika Olszewska
E-12	Dissecting the Immune Landscape of Mycosis Fungoides	Duncan J. Murray
	Scientific Session F. Biomarkers	
F-10	The Role of Matrix Metalloproteinase-2 Promoter Genotype and Its Immunohistochemical Expression with Specificity Protein-1 Transcription Factor in the Early Diagnosis of Mycosis Fungoides	Mona A-Halim Ibrahim
F-11	A microRNA based classifier in diagnosis and prognosis of cutaneous T cell lymphoma	Bo Wang
	Scientific Session G. Genetics	
G-09	Identification and validation of mitogen-activated protein kinase (MAPK) pathway gene muta- tions in Sézary Syndrome	Charlotte Flanagan
G-10	A large group of K111 pericentromeric human endogenous retroviruses are likely missing ("null K111") in patients with severe forms of cutaneous T cell lymphoma.	Trilokraj Tejasvi
	Scientific Session H. Cutaneous B-cell lymphomas	
H-06	Patch and thin plaque-type low-grade primary cutaneous B-cell lymphoma	Aviv Barzilai
H-07	Methotrexate-induced B-cell cutaneous lymphoma in erythrodermic cutaneous T-cell lymphoma patients.	Liliane Laroche
H-08	Rituximab monotherapy for primary cutaneous B-cell lymphoma: response and long-term fol- low-up in 24 patients	Constanze Jonak
H-09	Malignant Rosacea as a sign of systemic marginal zone lymphoma	Marie Beylot-Barry
H-10	Primary cutaneous follicular B cell lymphoma of the scalp associated with androgenetic alopecia in men	Joan Guitart
H-11	T-cell papulosis associated with B-cell malignancy: a distinctive clinicopathologic entity	Marie Beylot-Barry

Posters

ABSTRACTS PRESENTED AS ORALS WILL ALSO BE PRESENTED AS POSTERS USING THE NUMBERS REFERENCED IN THE SCIENTIFIC PROGRAM OF EVENTS

	Scientific Session I. Rare Cutaneous Lymphomas	
I-08	A single-centre experience of 9 patients diagnosed with blastic plasmacytoid dendritic cell neoplasm during a 5-year-period	Teresa Estrach Panella
	Scientific Session J: Quality of Life & Outcomes Studies	
J-06	Second Solid Organ Malignancies in Patients with Mycosis Fungoides in Greater Pittsburgh Area	Westley S. Mori
J-07	Comprehensive clinical data review of patients suffering from mycosis fungoides with bad out- come	Constanze Jonak
J-08	Skin infection in Mycosis fungoides and Sézary syndrome	Jinah Yoo
J-09	Prognostic factors in elderly patients with mycosis fungoides and sezary syndrome	Meenal Kheterpal
	Scientific Session K. Clinical Aspects	
K-06	Cutaneous Anaplastic Large Cell Lymphoma: A Comparative Clinical Feature and Survival Out- come Analysis of 52 Cases According to Primary Tumor Site	Woo Jin Lee
K-07	Subcutaneous Panniculitis Like T-cell Lymphoma: 15 Year Experience of the Greater Manchester Supra-Regional Cutaneous Lymphoma Multi-Disciplinary Team	Eileen Parry
K-08	An Evidence Based Approach to Refractory Sezary Syndrome	Asim Ahmad
K-09	Clinical Service evaluation of the new iPad skin weighted assessment tool (iSWAT)for patients with Mycosis Fungoides	Alex Kuciejewska
	Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation	
N-06	Extracorporeal photopheresis associated to multimodal therapy for T-cell cutaneous lymphoma	Marcia de Matos Silva
N-07	Extracorporeal photopheresis in the treatment of erythrodermic cutaneous T-cell lymphoma: a single centre long term experience	Ulrike Just
N-08	CD209+ monocyte-derived myeloid dendritic cells were increased in patients with leukemic cutaneous T-cell lymphoma after extracorporeal photopheresis	Xiao Ni
N-09	Late relapse of CTCL after allogeneic stem cell transplant: successful treatment with low dose interferon alpha and photopheresis.	Ellen J. Kim
N-10	Long-term clearance of blood and marrow involvement following graft failure and autologous reconstitution in a patient with Sézary syndrome who underwent allo-SCT	Giorgia Saporiti
N-11	Primary Cutaneous Large Cell Anaplastic Lymphoma: The Role of Brentuximab when the Out- look is Poor	Duncan J. Murray
N-12	Brentuximab vedotin in CD30+ cutaneous lymphoma: How do we treat - How shall we treat?	René Stranzenbach
N-13	Pembrolizumab Induces a Complete Skin and Blood Response in a Patient with Synchronous Sezary Syndrome and Metastatic Melanoma	Frederick Lansigan
N-14	Total Skin Electron Beam Therapy as Maintenance Skin-directed Therapy in Sezary Syndrome	Kerith E. Spicknall

Posters

ABSTRACTS PRESENTED AS ORALS WILL ALSO BE PRESENTED AS POSTERS USING THE NUMBERS REFERENCED IN THE SCIENTIFIC PROGRAM OF EVENTS

	Scientific Session O. Therapeutics 3: Endpoints & Clinical Trials	
O-11	First-in-Human, open label, multicenter phase 1 study of IPH4102, first-in-class humanized an- ti-KIR3DL2 mAb, in relapsed/refractory CTCL: preliminary results of exploratory biomarkers	Helene Sicard
	Scientific Session P: Clinical Management & Challenging Cases	
P-07	Folliculotropic Mycosis Fungoides: A Case Series Study	Alejandra Abeldaño
P-08	Early stage folliculotropic mycosis fungoides associated with eosinophilic pneumonia	Hanako Ohmatsu
P-09	Spontaneous remission of a pyogenic variant of a primary cutaneous CD30+ anaplastic large cell lymphoma in a young man	E. Geissler
P-10	Regression of a CD30-positive primary cutaneous T-cell lymphoproliferation after ribavirin treat- ment of chronic hepatitis E virus infection	Liliane Laroche
P-11	A Case of Primary Cutaneous Anaplastic Large Cell Lymphoma ALK- Negative	Rokhsareh Khatami
P-12	Prolonged survival in a 46-year-old male patient with cutaneous gamma/delta T-cell lymphoma	Ethan Sagher
P-13	Anaplastic large cell lymphoma involving skin and muscle associated with polymyositis	Tomomitsu Miyagaki
P-14	A case of angioinvasive cutaneous anaplastic large cell lymphoma completely regressed after low dose systemic methotrexate	Irene Russo
P-15	A Case of Subcutaneous Panniculitis-like T-cell Lymphoma Associated with Hemophagocytic Syndrome	Dhanalakshmi Balakrishnan
P-16	Livedoid vasculopathy as a possible clinical presentation of primary cutaneous lymphoma with a T regulatory phetotype.	Silvia Alberti-Violetti
P-17	Primary cutaneous follicle center lymphoma presenting as diffuse alopecia	Catherine G. Chung
P-18	Telangiectatic erythema induced by mechlorethamine gel (Valchlor)	Eve Maubec
P-19	Pralatrexate associated skin necrosis: a potential severe adverse effect	James Ko
P-20	Hair and Nail Changes in Patients with Mycosis Fungoids following Total Skin Irradiation	Debra L. Breneman
P-21	Transient Gynocomastasia as an Adverse Effect of Total Skin Electron Beam Irradiation for the Treatment of Cutaneous T-Cell Lymphoma	Debra L. Breneman
P-22	Maintenance phase in PUVA phototherapy of early stage Mycosis Fungoides. A critically ap- praised topic	Vieri Grandi

Abstracts * indicate

* indicates presenting author

SCIENTIFIC SESSION A: CLASSIFICATION & CLINICAL PATHOLOGY

A-01 STUDIES IN FOLLICULOTROPIC MF AND TRANSFORMED MF: CONSEQUENCES FOR THE ISCL/EORTC STAGING SYSTEM

ORAL Willemze R*1

¹Leiden University Medical Center, Leiden, the Netherlands

The ISCL/EORTC revision of the staging system for mycosis fungoides (MF) and Sezary syndrome (SS) published in 2007 recommends to document the presence of folliculotropic mycosis fungoides (FMF) and large cell transformation (LCT), since they may be associated with a worse prognosis and may require more aggressive therapies as compared to classic type MF. It also concluded that further data are required before modifications to the staging system are justified. In this presentation the results of recent published and unpublished studies addressing these issues and their consequences for the current staging system are discussed. Recent studies in FMF demonstrated that not all patients with FMF run a more aggressive clinical course compared with classic type MF. Clinicopathologic criteria were proposed that allow distinction between an indolent (early stage FMF) and a more aggressive (advanced stage FMF) subgroup. The 10-year disease specific survival of these two subgroups (93% vs 40%, respectively) was very similar to that reported in early and advanced stage classic MF. Recent studies indicating that patients with early stage FMF may benefit from standard skin directed therapies use in early stage classic MF are presented separately. Large cell transformation in MF has been associated with an aggressive clinical course and poor survival. However, a proportion of patients may run an indolent clinical course. Multivariate analyses of large cohorts of patients with transformed MF showed that negative staining for CD30, FMF, the extent of skin lesions showing transformation, transformation at extracutaneous sites and CDKN2A/2B deletions are independent predictors of reduced survival. However, in studies comparing patients with tumor stage classic MF (stage IIB) with or without LCT at first presentation, and similar studies in patients presenting with advanced stage FMF, no significant differences in survival were found. Taken together, the results of these studies may be helpful in predicting prognosis, in the selection of the most appropriate treatment, and in case of FMF may contribute to future modifications of the classification and staging system of MF/SS. The significance of LCT in patients with MF stage IIB, either at presentation or during follow-up, requires further study.

A-02 PRIMARY CUTANEOUS AGGRESSIVE EPIDERMOTROPIC T-CELL LYMPHOMAS: REAPPRAISAL OF A PROVISIONAL ENTITY IN THE 2016 WHO CLASSIFICATION OF LYMPHOMAS

ORAL Guitart J*¹, Martinez-Escala ME¹, Subtil A², Duvic M³, Pulitzer M⁴, Olsen E⁵, Kim E⁶, Wood GS⁷, Girardi M², Junkins-Hopkins J⁸, Ivan D³, Selim M⁵, Sable K¹, Virmani P⁵, Pincus L⁹, Tetzlaff M³, Kim J¹⁰, Kim YH¹⁰

Departments of Dermatology and Pathology: ¹Northwestern University Feinberg Medical School Chicago IL, ²Yale University, New Haven CT, ³MD Anderson Houston TX, ⁴Sloan Kettering Cancer Center, New York, NY, ⁵Duke University, Durham NC, ⁶University of Pennsylvania, Philadelphia PA, ⁷University of Wisconsin VAMC, Madison WI, ⁸Ackerman Academy New York, NY, ⁹University of California in San Francisco, San Francisco, CA, ¹⁰Stanford University, Stanford, CA

INTRODUCTION: Primary cutaneous CD8+ aggressive epidermotropic T- cell lymphoma (PCAETCL) is a rare and poorly characterized variant of cutaneous lymphoma still considered a provisional entity in the latest 2016 WHO Classification of Cutaneous lymphomas. We sought to better characterize and provide diagnostic and therapeutic guidance of this rare cutaneous lymphoma subtype. METHODS: We performed a retrospective review of our multicenter experience with PCAETCL. A group of dermatologists and dermatopathologist reviewed during two workshops clinical data, laboratory results and pathology materia of our combined PCAETCL experience.

RESULTS: Thirty-four patients with a median age of 76 years (range 19 - 89 years) presented primarily with extensive annular necrotic plaques or tumor lesions with frequent oral or perigenital involvement. The 5 year survival was 38.2% with a median survival of 12 months. A subset of 16 patients had a prodrome of chronic patches prior to the development of aggressive ulcerative lesions. None of the patients developed hemophagocytic syndrome or had significant co-morbidities. We identified cases with lack of CD8 or $\alpha\beta$ TCR expression yet with similar clinical and pathological presentation. Allogeneic stem cell transplantation provided the best results with 5 partial or complete remissions and 1 death.

CONCLUSIONS: We recommend expanding the definition of PCAETCL to include CD4/CD8 double negative cases and cases with $\alpha\beta/\gamma\delta$ TCR chain double expression. We have identified prodromic chronic patch lesions often misdiagnosed as eczema, psoriasis or MF that remain poorly characterized. Our experience confirms the poor prognosis of this entity and highlights AHSCT as the best option for a prolonged remission.

A-03 PRIMARY CUTANEOUS CD8-POSITIVE AGGRESSIVE EPIDERMOTROPIC CYTOTOXIC T-CELL LYMPHOMA: CLINI-CO-PATHOLOGICAL FEATURES AND GENOMIC ALTERATIONS

ORAL Fanoni D¹, Alberti-Violetti S¹, Corti L1, Venegoni L², Merlo V¹, Bernareggi S³, Onida F², Berti E^{*2}

¹U.O.C. Dermatologia-Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Milan, Italy, ²Università degli Studi di Milano, Milan, Italy, ³Università degli Studi di Milano-Bicocca, Milan, Italy

Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma (AETCL) is a rare peripheral T-cell lymphoma with an aggressive behavior (overall survival 12-32 months). Differential diagnosis, made with other indolent CD8 positive lymphomas, such as Lymphomatoid papulosis type D and CD8 positive Mycosis fungoides, is important because of prognosis and therapeutic choices. We retrospectively evaluated clinical aspects and histological features in 15 patients affected by AETCL. Ka-

Abstracts

SCIENTIFIC SESSION A: CLASSIFICATION & CLINICAL PATHOLOGY

plan-Meier estimate was used to determinate the overall survival (OS). Array-comparative genomic hybridization (aCGH) analysis was performed to evaluate the genomic profile. Two clinical presentations were found: 1) diffuse ulcerated and eruptive papules, nodules and tumors; 2) localized nodules, tumors or plaques, especially on acral sites. Histologically, the typical cytotoxic CD8+ neoplastic infiltrate showed a lichenoid pattern with marked epidermotropism in the diffuse variant, but it is more dense and deeper with less epidermotropism in the localized variant. Median OS was 10 months, without any significant differences between two groups. Twelve patients (80%) died for lymphoma, 1 died for heart failure. One patient is lost to follow-up and only 1 patient is alive with the disease. aCGH analysis revealed a complex profile mainly characterized by numerous gains, whose frequency was higher than 80% on chromosome 7q and 17q. The most frequent loss (>80%) was on 9p21 region, in particular on CDKN2A and CDKN2B loci. AETCL is characterized by two clinic-pathological variants but the same aggressive course. Genomic analysis showed the same and peculiar profile in all cases. Alterations were numerous as reported in aggressive neoplasms.

A-04 CD8+ MYCOSIS FUNGOIDES: AN INDOLENT LYMPHOPROLIFERATIVE DISORDER

ORAL Martinez-Escala ME*, Kantor RW, Cices A, Choi J, Guitart J Departments of Dermatology, Northwestern University, Feinberg Medical School, Chicago, IL

CD8+ mycosis fungoides (MF) is an uncommon CTCL variant observed in young patients and characterized by dyschromic patches and an indolent course. We reviewed our experience with CD8+ MF presenting in pediatric and adult population. This is a retrospective review of patients diagnosed with CD8+ MF at our institution between 1995 and 2016. Clinical data and skin biopsies of all eligible patients were collected and reviewed. Only patients with length of follow-up of at least 3 years were included in evaluation of prognosis. Fifty-two patients were included (31 male, 21 female) which correspond to approximately 5% of MF cases in our database. The median age was 25 years (2-76) with 21 patients (40.4%) younger than 21 years. At presentation 47% were stage IA and 53% stage IB. Caucasians presented with erythematous patches (20 patients) while hypopigmented patches (10 patients) were more frequent among patients with dark complexion. Follow up was available in 32 patients with a median duration of 7.4 years (3.1 - 21.2). Complete remission was achieved in 26 patients (61.9%), however recurrence was reported in 8 patients, with a median time to relapse of 19.4 months (14.7 - 25.4). Progressive disease was observed in two patients, which was only limited to more than 50% increase of patch surface area. None of the patients developed thick plaques, tumors, nodal or systemic involvement. All biopsies were diagnostic of MF. Scattered necrotic keratinocytes were seen in 7/40, Pautrier microabcesses were rare (4/40) and folliculotropism not observed. The most common phenotype was CD3+ (21/28), CD8+ (52/52), CD4- (49/50), CD7+ (7/26), CD5+ (10/15), CD30+ (6/9), βF-1+ (5/7), GM1 (γ3.20 clone)- (6/8), CD56- (9/11), TIA-1+ (8/12) and CD45RA+ (7/8). This is largest series of cases of CD8+ MF confirming the indolent course of this condition. Once CD8+ PCAETCL and dermal CD8+ CTCL variants have been excluded, patch presentation of CD8+ MF does not seem to progress into tumor stage or systemic disease. Therefore, we suggest that CD8+ MF should be classified as a lymphoproliferative condition rather than a bona fide lymphoma.

A-05 UNILESIONAL MYCOSIS FUNGOIDES IS ASSOCIATED WITH INCREASED EXPRESSION OF MIR-17~92, TH1 CYTO-KINE PROFILE AND ABSENCE OF TH2

ORAL Moyal L*^{1,2}, Yehezkel S^{1,2}, Gorovitz B^{1,2}, Rotem C^{1,2}, Jacob-Hirsch J³, Sherman S^{1,2}, Barzilai A⁴, Feinmesser M⁵, Hodak E^{1,2} ¹Laboratory for Molecular Dermatology, Felsenstein Medical Research Center, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ²Department of Dermatology, Rabin Medical Center, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ³Cancer Research Center, Sheba Medical Center, Tel Hashomer, Israel; ⁴Department of Dermatology, Sheba Medical Center, Tel Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ⁵Institute of Pathology, Rabin Medical Center, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Unilesional mycosis fungoides (MF) is a rare variant of cutaneous T-cell lymphoma. It is characterized by a solitary lesion that is clinicopathologically indistinguishable from conventional patch/plaque MF and has an excellent prognosis. The cytokine and microR-NA expression profiles of unilesional MF have not yet been investigated. Previous studies have shown that the miR-17~92 cluster (miR-17, 18a, 19a, 19b, 20a, 92a) is involved in lymphocyte development and in remodeling the T-cell anti-cancer immune defense towards a Th1 response, with suppression of Th2. The aim of the study was to investigate the role of microRNAs in the pathogenesis of unilesional MF. Biopsy samples of unilesional MF, early MF, tumor MF, and inflammatory dermatoses were studied for microRNA expression using the Affymetrix microRNA array. Findings were validated by qPCR with the ABI platform. The expression of miR-related genes as well as immune markers was evaluated with NanoString technology. Cytokine protein expression was assessed by immunohistochemistry using antibodies against GATA-3 (Th2 marker). The unilesional MF samples (n=18) were characterized by significantly higher expression levels of miR-17, miR-18a, and miR-20a than samples of early MF (n= 24), tumor MF (n=10), and inflammatory dermatoses (n=14), and a significantly increased expression of Th1-related genes (IL2, IL12B, IFN-y, CD49b and CCR10) than early MF samples. Unilesional MF biopsies were completely negative for GATA-3 whereas dermal lymphocytes of early MF were positive for GATA-3. A high expression of miR-17~92 and Th1 cytokines, with negative GATA-3 protein expression, distinguish unilesional MF from early MF. We suggest that the miR-17~92 cluster plays a role in the localized nature of unilesional MF by mediating the Th1 anti-cancer response together with suppression of Th2. Further studies are required to validate the link between miR-17~92 and the immune profile of Th1 against cancer cells.
SCIENTIFIC SESSION A: CLASSIFICATION & CLINICAL PATHOLOGY

A-06 PEDIATRIC MYCOSIS FUNGOIDES: CLINICOPATHOLOGIC CHARACTERISTICS AND OUTCOME AND A STUDY OF THE HUMAN LEUKOCYTE ANTIGEN SYSTEM

ORAL Reiter O¹, Ben Amitai D², Amitay-Laish I¹, Israeli M³, Pavlovsky L¹, Hodak E^{*1}

¹Department of Dermatology, Rabin Medical Center-Beilinson Hospital, Petach Tikva; ³Tissue Typing Laboratory, Rabin Medical Center-Beilinson Hospital, Petach Tikva; ²Dermatology Unit, Schneider Children's Medical Center, Petach Tikva; Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

The literature on mycosis fungoides (MF) in children/adolescents is sparse, and the published series are limited by small number of patients and by relatively short follow-up periods. The detection of certain human leukocyte antigen (HLA) alleles in adults with MF in some populations, including Israeli Jewish patients, might indicate an underlying immunogenetic mechanism in the pathogenesis of the disease. The aim of this study was to summarize our experience with pediatric MF in a larger series than included in our previous report, with emphasis on long-term outcomes, and to study the possible association with the HLA system. The cohort included 71 Jewish patients with MF aged <18 years at diagnosis. Their files were reviewed, and the patients were invited for a follow-up visit. High-resolution genotyping of HLA class I (HLA-A*, and-B*) and HLA class II (HLA -DRB1*, DQA1* and DQB1*) loci was performed in 59 patients who gave consent. There were 45 male (63%) and 26 female patients, of average age 8 years at symptom onset and 11 years at diagnosis. All but 2 had early-stage disease at presentation, mainly hypopigmented (44%), folliculotropic (42%), and classical MF (39%), alone or in combination. Mean follow-up time was 6.1 years (range 0.3-18 years); 31 patients (44%) were followed beyond age 18 years. Complete response was achieved by 81.5% of patients after an average of 1.6 treatment modalities, and it was followed by at least one relapse in 79% of cases. Stage progression occurred in 3 patients: from IA to IB/IIA in 2 and to advanced stage in adulthood in 1. None of the allele frequencies of any of the tested HLA loci deviated from controls. Our findings highlight the distinct clinical nature of pediatric MF compared to adult MF. Pediatric MF also follows a more indolent course even over a relatively long follow-up period. It seems that pediatric MF lacks the significant associations with the HLA system reported in adult MF, suggesting that it may have a different patho-immunogenetic basis.

A-07 PSORIASIS IN PATIENTS WITH MYCOSIS FUNGOIDES: A CLINICOPATHOLOGIC STUDY OF 25 PATIENTS

POSTER Nikolaou V, Marinos L, Papadavid E, * Economidi A, Christofidou E, Karambidou K, Tasidou A, Ekonomaki E, Stratigos A, Antoniou C

"Andreas Sygros" Hospital for skin diseases, Cutaneous Lymphoma Clinic, 5 I. Dragoumi str, 16121, Athens Greece; "Evangelismos Hospital", Hemopathology Department, 45-46 Ipsilandou str, 10676, Athens, Greece

INTRODUCTION: It has been reported that patients with psoriasis are at an increased risk of developing lymphomas. The objective of the current study was to investigate the association between mycosis fungoides (MF) and psoriasis.

METHODS: All MF patients diagnosed and followed from January 2005 to December 2015 who carried both MF and psoriasis diagnosis were retrospectively evaluated. Cases diagnosed with MF with histologically confirmed psoriasis and cases with MF who carried a strong clinical history of psoriasis ie typical clinical presentation and/or respond to anti-psoriatic treatments (cyclosporine and/or anti-TNFα) were included. Histological criteria for psoriasis included presence of Munro microabscesses, partial or complete loss of granular layer, neutrophil exocytocis, uniformly elongated rete ridges with accompanying hyper- and/or parakeratosis. Histological criteria for MF were standard morphology (atypical cells with epidermotropic or folliculotropic features) and immuno-histochemically uniform expression of CD4, or loss of other T-cell markers, regardless of the presence of other features consistent with psoriasis diagnosis.

RESULTS: Forty-one out of the 321 patients diagnosed with MF carried also a diagnosis of psoriasis on their medical records. Twenty-five (7.8%) met the inclusion criteria. Fourteen patients had psoriatic lesions at the time of MF diagnosis. In 20 patients there was histological confirmation of both diseases. Five patients (20%) were diagnosed with folliculotropic MF whereas another 5 patients presented with palmoplantar and nail psoriasis (histologically confirmed in 4 of them). In 4 patients there was a very close temporal relationship to the diagnosis of MF and psoriasis. Thirteen patients with psoriasis history had been treated with immunomodulatory therapies (7 patients who treated with anti-TNF α and 10 patients treated with cyclosporine). Interestingly, in 9 patients classic histologic findings of both diseases were detected in the same biopsy.

CONCLUSIONS: Our results support that the association between psoriasis and MF exists and is probably related to chronic lymphocyte stimulation in psoriasis which eventually leads to a dominant clone and evolution to CTCL. Our study supports that although to date we believed that early MF is often misdiagnosed as psoriasis, there are cases where there is coexistence or progression of the disease to MF.

SCIENTIFIC SESSION B: PATHOGENESIS & APOPTOSIS

B-01 APOPTOTIC ABNORMALITIES IN CTCL: PATHOGENETIC AND THERAPEUTIC IMPLICATIONS

ORAL Wood GS*, Wu J, Salva KA

Department of Dermatology, University of Wisconsin and VAMC, Madison, WI, USA

INTRODUCTION: We have shown that CTCL (MF/SS) cases often harbor defective activation-induced cell death (AICD) and other extrinsic apoptotic pathway abnormalities that allow tumor cells to persist and acquire additional somatic abnormalities leading to enhanced proliferation. Rather than focusing on blockade of these acquired proliferative drivers that can be highly diverse and variable, we have explored ways to promote tumor cell death by manipulation of the more restricted repertoire of apoptotic pathways. METHODS: In-vitro, ex-vivo and in-situ quantitative analysis of apoptosis and apoptotic factor DNA methylation, mRNA and protein using flow cytometry, pyrosequencing, QRT/PCR, immunoblots and multispectral imaging.

RESULTS: First, we have documented a progressive increase in c-CBL (an E3 ubiquitin ligase that down-regulates receptor-associated tyrosine kinases) across the spectrum of T-cells in normal tissue, chronic dermatitis and CTCL. si-RNA knockdown of c-CBL enhances T-cell receptor signaling leading to increased FAS-ligand (FASL) and subsequent AICD in CTCL cases expressing adequate FAS death receptor. In cases with low baseline FAS, pretreatment with methotrexate (MTX) reduces methylation of the FAS promoter thereby derepressing FAS and augmenting AICD. A search is now underway for small molecule inhibitors of c-CBL. Second, by a similar epigenetic mechanism and perhaps others, pretreatment with MTX enhances the apoptotic effect of photodynamic therapy (PDT) on the FAS and TRAIL branches of the extrinsic apoptotic pathway. We refer to this as epigenetically-enhanced PDT (ePDT). Third, we performed high-throughput screening of >1,700 small molecules and discovered that gentian violet (an inexpensive tissue stain, antimicrobial agent and NOX/ANG2 inhibitor) effectively kills CTCL cells in association with enhanced FAS- and TRAIL-mediated apoptosis. In 1/1 case, topical application of 2% aqueous gentian violet daily cleared patches/thin plaques of MF within one month without side effects.

CONCLUSIONS: In aggregate, these advances support a key role of apoptotic abnormalities not only in the pathogenesis of CTCL but also chronic dermatitis, and may help explain the apparent evolution of some cases of CTCL from chronic dermatitis. They also provide novel, cost-effective therapeutic options for MF/SS patients, each option best suited to particular clinical situations.

B-02 MICRO RNA REGULATORY CIRCUITS IN CHEMOTHERAPY-INDUCED APOPTOSIS IN CTCL CELLS

ORAL Gniadecki R*1

¹Department of Dermatology, University of Copenhagen, Denmark and University of Alberta, Canada

INTRODUCTION: In an in vitro model of chemotherapy-induced apoptosis in CTCL lines, a wide range of drugs or PUVA induced programmed cell death via inhibition of Akt signaling and activation of p53. However, complete apoptosis could not be achieved even after prolonged incubation in media containing high concentration of drugs. We have therefore speculated that drugs induce protective regulatory pathways in lymphoma cells increasing resistance to apoptosis.

METHODS: CTCL lines MyLa, SeAx and HuT-78 were incubated with various chemotherapeutics (doxorubicin, bortezomib, etoposide, gemcitabine, gamma-secretase inhibitors) or subjected to in vitro PUVA. Changes in micro RNA expression were measured by microarrays and selected micro RNAs were then assayed by PCR. Transfection with miRNA mimics or inhibitors was performed to assess the impact on apoptosis, measured by flow cytometry (PI exclusion and annexin V surface expression).

RESULTS: We identified miR-125b and miR-122 as regulators of apoptosis in CTCL cells. Both species are expressed in mycosis fungoides in vivo and exerted anti-apoptotic effect in vitro. SCID mice transplanted with MyLa cell line overexpressing miR-125b developed larger tumors and had shorter survival than the control. Detailed analysis of the mechanism of action revealed that miR-125b targeted MXD4/MAD and activated c-myc signaling. In contrast, miR-122 was induced primarily by p53 and enhanced Akt phosphorylation

CONCLUSIONS: In CTCL cells micro RNAs are engaged in the negative regulatory loop signaling protecting against apoptosis. We generalize our findings to propose a mechanism of apoptosis regulation via two self-augmenting proapoptotic signaling loops and one antiapoptotic circuit. Further mathematical analysis by Gray-Scott reaction-diffusion modelling predicted existence of islands of tumor cells that remain protected from apoptosis even in presence of very high concentrations of drugs.

Acknowledgement: Data used in this study have been generated in Gniadecki's laboratory in collaboration with the following researchers: Valentina Manfé, PhD, Edyta Biskup, PhD, Maria Kamstrup, MD, PhD, Niels Ødum, MD, PhD, Cecilia Savorani, PhD, Carlo M Croce, PhD.

Abstracts **

* indicates presenting author

SCIENTIFIC SESSION B: PATHOGENESIS & APOPTOSIS

B-03 INVESTIGATING THE ROLE OF PLCG1 MUTATIONS IN SÉZARY SYNDROME

ORAL Patel VM*¹, Woollard WJ¹, Yoxall A¹, Begum N¹, Katan M², Whittaker SJ¹ Mitchell TJ¹ ¹St John's Institute of Dermatology, Division of Genetics and Molecular Medicine, King's College London, SE1 9RT; ²Structural and Molecular Biology, Division of Biosciences, University College London, WC1E 6BT

INTRODUCTION: We and others have identified *PLCG1* (encoding PLCy1), a mediator of T-cell Receptor (TCR) signalling, to be a highly mutated gene in up to 21% of Cutaneous T-cell Lymphomas, 13% of Peripheral T-cell Lymphomas and 36% of Adult T-cell Leukaemia/Lymphomas. This study aimed to functionally interrogate *PLCG1* aberrations (p.R48W, p.S312L, p.D342N, p.S345F, p.S520F, p.R1158H, p.E1163K, p.D1165H and p.VYEEDM1161V) identified in Sézary Syndrome.

METHODS: Site-directed mutagenesis was used to generate mutant *PLCG1* constructs. HEK293 cells were transfected with *PLCG1* vectors and protein expression was analysed by western blotting. Protein activity was investigated by co-transfecting HEK293 cells with NFAT-firefly luciferase or NFκB-firefly luciferase reporter plasmids, a Renilla luciferase transfection control vector and *PLCG1* constructs. Cell lysates were analysed with dual luciferase reporter assays and statistical significance was assessed by two-tailed Student's t-test. Mutations were mapped onto the PLCβ2 structure (PDB: 2ZKM) using Pymol.

RESULTS: Seven mutant PLCv1 proteins had comparable expression to wild-type protein. Interestingly, PLCv1_R1158H and PLCv1_ VYEEDM1161V mutant proteins showed reduced expression compared to wild-type PLCv1. Luciferase reporter assays revealed that all mutations, except p.R1158H, significantly increased NFAT and NFkB transcriptional activity. The p.D342N, p.S345F, p.S520F, p.E1163K, p.D1165H and p.VYEEDM1161V mutations increased NFAT activation 6.5 – 12.0 fold ($p \le 6x10^{-6}$) and NFkB activation 2.9 - 10.8 fold ($p \le 1.3x10^{-5}$). These findings confirm that p.S345F, p.S520F increase NFAT activation as shown by Vaqué *et al.* (2014). Interestingly, protein modelling of p.D342N, p.S345F, p.E1163K, p.D1165H and p.VYEEDM1161V demonstrates they are located on the exterior surface of PLCv1 and are predicted to interact with the plasma membrane, where the substrate of PLCv1, PIP₂, is located.

CONCLUSIONS: This study shows that the *PLCG1* mutations p.R48W, p.S312L, p.D342N, p.S345F, p.S520F, p.E1163K, p.D1165H and p.VYEEDM1161V are potent mediators of gain-of-function, through increased NFAT and NFkB transcriptional activity. The p.D342N, p.S345F, p.E1163K, p.D1165H and p.VYEEDM1161V mutations are predicted to interact with the plasma membrane, therefore may increase PIP₂ hydrolysis and enhance TCR signalling to drive the molecular pathogenesis of Sézary Syndrome. Thus, *PLCG1* mutations may represent novel therapeutic targets for small molecule inhibitors.

B-04 A COMPARISON OF TRANSCRIPTOME SEQUENCING AND TOX DamID SEQUENCING DATA IDENTIFIES PUTATIVE DOWNSTREAM EFFECTS OF TRANSCRIPTION FACTOR DYSREGULATION IN SÉZARY SYNDROME

ORAL Dulmage BO*¹, Akilov O², Vu JR², Falo, LD Jr.², Geskin LJ²

¹Department of Dermatology, Northwestern University, Chicago, Illinois, USA, ²Department of Dermatology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA, ²Department of Dermatology, Columbia University, New York, New York, USA

INTRODUCTION: We previously demonstrated that *TOX*, a transcription factor not normally expressed in mature lymphocytes, is upregulated in Sézary syndrome CD4+ T-cells. Here, we sought to further characterize the downstream effects of TOX upregulation. METHODS: We used siRNA to suppress TOX expression and characterized the effect on cell viability as well as expression of the known downstream targets of *TOX* before and after using qRT-PCR. To expand the search for putative effects of TOX overexpression in SzS, we compared our list of dysregulated genes from sequence-based transcriptome analysis to the results of a TOX DamID sequencing study by Artegiani et al. (2015) that identified TOX binding sites in the human genome. We used Ingenuity Pathway Analysis to identify common pathways and molecules both altered in SzS and affected by the binding of TOX.

RESULTS: Previously, we identified downregulation of *RUNX3*, a tumor suppressor that modulates the strength of Wnt signaling by complexing with β -catenin and T-Cell Factor 4, a *GATA3* a known effector of RUNX3 in SzS. TOX and RUNX3 expression are significantly inversely proportional, and TOX knockdown rescues RUNX3 expression and reduces cell viability. Our comparison of dysregulated genes in SzS and TOX binding sites revealed 2069 genes on both lists including RUNX3 as well as other genes our group and others have studied such as GATA3, EPHA4, SATB1, NEDD4L, and CDKN2A. Further, many members of the Wnt/ \mathbb{P} -catenin signaling pathway are sites of TOX binding. Moreover, four histone deacetylases were found on both lists.

CONCLUSIONS: As a transcription factor, TOX dysregulation in SzS can in turn lead to downstream changes in expression of other genes related to disease pathogenesis. Our qRT-PCR data supports the conclusion that TOX suppresses RUNX3 in SzS cells. Further, TOX binding at RUNX3 was demonstrated by Artegiani et al. (2015) in their DamID sequencing work. Additional comparison of genes differentially expressed in SzS and those bound to TOX revealed more putative effects of TOX overexpression.

SCIENTIFIC SESSION B: PATHOGENESIS & APOPTOSIS

B-05 INACTIVATION OF RUNX3/P46 PROMOTES CUTANEOUS T-CELL LYMPHOMA

ORAL Haider A¹, Steininger A², Ullmann R^{2,3}, Hummel M⁴, Dimitrova L⁴, Beyer M¹, Vandersee S^{1,5}, Lenze D⁴, Sterry W¹, Möbs M,^{1,4} Assaf C^{*1,6}

¹Department of Dermatology, Charité – Universitaetsmedizin Berlin, Berlin, Germany; ²Max Planck Institute for Molecular Genetics, Berlin, Germany; ³Institut für Radiobiologie der Bundeswehr in Verbindung mit der Universität Ulm, Munich, Germany; ⁴Institute of Pathology, Charité – Universitaetsmedizin Berlin, Berlin, Germany; ⁵Central German armed forces hospital, Department of Dermatology and Allergy, Koblenz, Germany; ⁶Department of Dermatology, HELIOS Klinikum Krefeld, Krefeld, Germany

INTRODCUTION: The key role of the Runt-related transcription factor 3 (RUNX3) in physiological T-cell differentiation has been extensively documented. However, information on its relevance for the development of human T-cell lymphomas or leukemias is scarce.

METHODS: CTCL cell lines and highly purified tumor cells as well as skin samples from 26 patients having Sézary syndrome were analysed by array CGH, methylation analyses, DNA sequencing. Findings were confirmed by Western blotting, immunohistochemistry and FISH analyses. In addition functional analyses were following as nucleotransfection and apoptosis- and proliferation assays. RESULTS: Here we show that alterations of *RUNX3* by either heterozygous deletion or methylation of its distal promoter can be observed in the tumor cells of 15/21 (71%) patients suffering from Sézary syndrome (SS), an aggressive variant of cutaneous T-cell lymphoma. In consequence, mRNA levels of RUNX3/p46, the isoform controlled by the distal promoter, are significantly lower in SS tumor cells. Re-expression of RUNX3/p46 promotes apoptosis and slows down proliferation in a RUNX3/p46^{low} cell line of cutaneous T-cell lymphoma.

CONCLUSIONS: By this we present the first evidence that RUNX3 can act as a tumor suppressor in a human T-cell malignancy and suggest that this effect is predominantly mediated through transcripts from its distal promoter, in particular RUNX3/p46.

B-06 STAT3 ACTIVATION RESULTS FROM THE EPIGENETIC ABROGATION OF MIR-124 IN CUTANEOUS T-CELL LYMPHOMA

ORAL Gallardo F*, García L, Sandoval J, Díaz-Lagares A, González J, Servitje O, Estrach T, Espinet B, Bellosillo B, Pujol RM, Bigas A, Espinosa L

Department of Dermatology, Institut Hospital del Mar d'Investigacions Mèdiques (IMIM), Universitat Autònoma de Barcelona, Cancer Research Program. Translational Medical Oncology, Health Research Institute of Santiago (IDIS), Complexo Hospitalario Universitario de Santiago de Compostela, SERGAS. Epigenomics Unit, IIS, La Fe-Valencia. Stem Cells and Cancer Research Laboratory-IMIM. Department of Dermatology, Hospital de Bellvitge. Citogenètics and Molecular Biology Laboratory, Department of Pathology-Hospital del Mar. Barcelona, Spain.

INTRODUCTION: Increasing evidences support a potential role for the Signal Transducer and Activator of Transcription-3 (STAT3) as a tumor driver in cutaneous T-cell lymphoma (CTCL). However, the mechanisms leading to STAT3 pathway activation in CTCL and how STAT3 activation contributes to lymphomagenesis remains primarily unexplored. Recently, we found that miR-124, known to regulate STAT3, is robustly silenced in mycosis fungoides (MF) tumor-stage and CTCL cell lines. A possible deregulation of miR-124 as a contributing factor to STAT3 pathway activation in CTCL was evaluated.

METHODS: DNA methylation status of miR-124 and its expression levels in response to the DNA-demethylating agent azacitidine were evaluated in MF tumor samples and CTCL cell lines (Myla, HuT-78, SeAx and HH). CTCL cell lines were infected with a lentiviral vector encoding miR-124. Transduced cells were selected in puromycin containing medium and analyzed by western blot for P-STAT3 and STAT3 levels. The impact of STAT3 signaling using specific STAT3 inhibitors on CTCL cell lines and primary Sézary cells was evaluated.

RESULTS: A significant promoter methylation and silencing of the STAT3-related miR-124 in MF tumor samples and CTCL cell lines was detected. Downregulation of miR-124 in CTCL was associated with high levels of STAT3 that were significantly reduced by ectopic miR-124 expression. Selective blocking of STAT3 signaling resulted in decreased cell growth, indicating the relevance of STAT3 pathway activation CONCLUSIONS: Our study deciphers novel epigenetic mechanisms regulating STAT3 pathway in CTCL, which might contribute to a better understanding of the molecular basis of CTCL development. Deregulation of STAT3 signaling has a major impact on cell survival in both CTCL cell lines and primary Sézary cells indicating the potential interest of STAT3 as a therapeutic target for CTCL.

SCIENTIFIC SESSION B: PATHOGENESIS & APOPTOSIS

B-07 NOVEL HIGH-THROUGHPUT VIROME CAPTURE SEQUENCING TECHNIQUE TO IDENTIFY VIRAL PATHOGENS IN PATIENTS WITH CUTANEOUS T-CELL LYMPHOMA

ORAL Anderson ME1*, Nagy-Szakal D², Jain K², Frattini MG³, Lipkin WI², Geskin LJ¹

¹Department of Dermatology, Columbia University Medical Center, New York, NY; ²Center for Infection and Immunity Mailman School of Public Health of Columbia University New York, NY; ³Department of Medicine, Columbia University Medical Center, New York, NY

INTRODUCTION: Sézary Syndrome (SS) is a variant of cutaneous T cell lymphoma (CTCL) characterized by leukemic involvement. The SS pathogenesis is still poorly understood, but chronic antigen stimulation due to a bacterial or viral infection or colonization of the skin may lead to malignant transformation of the skin resident T cells. All efforts to implicate oncogenic viruses have yielded inconsistent results. We used specific virome capture sequencing platform for vertebrate viruses (VirCapSeq-VERT), a novel and highly sensitive viral detection technique, to search for viral sequences in malignant T cells isolated from serum samples of SS patients.

METHODS: VirCapSeq-VERT was used to identify viral sequences in malignant T cells isolated from six SS patients [5 females, 1 male; age: 60-82 years]. Total nucleic acids from plasma and peripheral blood mononuclear cells (PBMC) were extracted and sequencing was done with Illumina MiSeq platform. The sequenced reads were *de novo* assembled and subjected to homology search using MegaBLAST against the GenBank nucleotide database and BLASTx against the GenBank protein database.

RESULTS: In total, 27 million paired-end reads were generated using Illumina MiSeq, with an average of 2.25 million paired-end reads per sample. Of these, 49,349 sequences showed homology to 23 unique viral species. Assembled contigs and unassembled reads were further mapped to reference genomes identified from blast to assess genome coverage and depth. Sequences from human endogenous retrovirus–K (HERV-K) and human T-lymphotropic virus 1 (HTLV-1) were detected in each sample. Polymerase chain reaction (PCR) screening was negative for a panel of viruses that had previously been linked to CTCL.

CONCLUSIONS: Short sequences from HERV-K and HTLV-1 were found in all six patient samples. These sequences closely matched sequences found in the human genome, and further investigation is necessary to determine whether these proviral particles may represent pathologic sequences.

B-08 MITOCHONDRIAL RETROGRADE SIGNALING REGULATES SENSITIVITY TO METABOLIC STRESS AND ALLOWS SE-LECTIVE TARGETING OF CUTANEOUS T-CELL LYMPHOMA

ORAL Anshu A, Kittipongdaja W, Schieke SM*

Departments of Dermatology, University of Wisconsin-Madison, Madison, USA & Medical College of Wisconsin, Milwaukee, USA

INTRODUCTION: Tumor cell metabolism is widely studied to identify cancer-specific aberrations in metabolic pathways serving as novel treatment targets. However, the high degree of metabolic plasticity allowing cancer cells to adapt to changes in tumor microenvironment decreases sensitivity to metabolic drugs. Herein, we characterize the molecular events "rewiring" metabolism in response to mitochondrial bioenergetic stress and uncover potential therapeutic targets in neoplastic T-cells.

METHODS: The effects of phenformin, an inhibitor of mitochondrial respiration, on metabolism, cell growth, and survival in vitro and in xenograft tumors were examined in the neoplastic T-cell lines, Hut78, HH, Jurkat, in comparison to normal T-cells from healthy donors.

RESULTS: Inhibition of mitochondrial respiration led to an enhanced Warburg effect inducing a glucose-dependent phenotype with upregulation of aerobic glycolysis in lymphoma cells which was not seen in normal T-cells. After treatment with phenformin, cells demonstrated increased generation of mitochondrial reactive oxygen species (mitoROS) functioning as a cytoprotective signal with the antioxidants N-acetylcysteine (NAC) and mitoTEMPO disrupting metabolic reprogramming and survival. In a mouse model, NAC synergized with phenformin to block growth of xenograft tumors. Neoplastic T-cells unlike normal T-cells showed a mitoR-OS-dependent stabilization of HIF-1a in response to inhibition of mitochondrial respiration which was critical to glycolytic reprogramming and survival of lymphoma cells. Suppression of HIF-1a blocked metabolic plasticity and led to marked apoptotic death after phenformin. A xenograft tumor model confirmed the synergistic effect of phenformin and genetic or small molecule-induced suppression of HIF-1a with markedly reduced tumor size only in the combination group.

CONCLUSIONS: We describe a previously unreported role of mitochondrial retrograde signaling, an evolutionary conserved pathway linking mitochondrial stress and lifespan in lower organisms, in reprogramming cellular metabolism upon inhibition of mitochondrial respiration. Our results identify redox-dependent HIF-1a signaling as a critical factor in the resistance of T-cell lymphoma cells against the mitochondrial inhibitor phenformin. Inhibition of the mitoROS/HIF-1a axis disrupted metabolic plasticity and survival in response to phenformin allowing selective targeting of lymphoma cells.

Scientific Session C: Multinational Collaborative Studies

C-01 CUTANEOUS LYMPHOMA INTERNATIONAL CONSORTIUM: AN ADVANCED STAGE PROSPECTIVE STUDY UNITING INTERNATIONAL EXPERT CENTRES TO EVALUATE AND VALIDATE THE PROGNOSTIC INDEX MODEL

ORAL Scarisbrick JJ*1*, Quaglino P², Vermeer M³, Whittaker S⁴, Wood GS⁵, Duvic M⁶, Prince HM⁷, Horwitz S⁸, Hoppe R⁹, Porcu P¹⁰, Stadler R¹¹, Guitart J¹², Gru A¹³, Bagot M¹⁴, Olsen E¹⁵, Hodak E¹⁶, Evison F¹, and Kim YH¹⁷

¹University Hospital Birmingham, Birmingham, UK, ²University of Turino, Turino, Italy; ³Leiden University Medical Centre, Leiden, Netherlands; ⁴Kings College London, St John's Institute of Dermatology, London, UK, ⁵University of Wisconsin, Madison, WI, USA; ⁶The University of Texas, MD Anderson Cancer Center, Houston, Texas., USA; ⁷Peter MacCallum Cancer Centre, Melbourne, Australia; ⁸Memorial Sloan Kettering Cancer Center, New York, NY; ⁹Stanford University School of Medicine, Stanford, CA; ¹⁰The Ohio State University, Columbus, Ohio, USA, ¹¹Johannes Wesling Medical Centre, Minden, Germany; ¹²Northwestern Memorial Hospital, Chicago, USA, ¹³University of Virginia, Charlottesville, Virginia, USA, ¹⁴Hospital St Louis, Paris, France, ¹⁵Duke University, Durham, North Carolina, USA, ¹⁶Rabin Medical Center, Tel Aviv, Israel, ¹⁷Stanford University, Stanford, CA, USA.

INTRODUCTION: The Cutaneous Lymphoma International Consortium (CLIC) is a collaborative group of international cutaneous lymphoma experts which aims to generate large-scale projects for the improvement of patient management and outcomes. CLIC demonstrated the feasibility of such collaboration in a retrospective study in advanced mycosis fungoides (MF) and Sézary syndrome (SS) that screened 10 candidate prognostic parameters in 1275 patients from 29 international sites¹. Four independent prognostic markers associated with a poor survival were identified (stage IV, age of diagnosis >60 years, large-cell transformation in skin and raised lactate dehydrogenase). Using these 4 parameters together in a prognostic model identified three risk groups across stages IIB-IVB with significantly different 5-year survival rates: low risk (68%), intermediate risk (44%), and high risk (28%). We hope that a risk-stratified management approach may improve survival outcome.

METHODS: There are intrinsic flaws of retrospective analysis and prognostic models require validation prospectively and this allows newer prognostic factors to be evaluated. As such a prospective study to evaluate and validate relevant prognostic factors in advanced-stage MF/SS is underway. All registered patients are subject to a central pathological review to confirm correct diagnosis. A federated biobank where clinical samples are linked with rigorous clinical annotation is available for translational research.

RESULTS: This CLIC study on advanced-stage MF/SS is now open in Europe and other CLIC centers are expected to start this study later this year. To date, 66 patients, 38 males and 28 females (male to female ratio 1.4:1) including 41 with advanced stage MF and 25 with SS patients have been enrolled. Stages IIB;n=21, IIIA;n=5, IIIB;n=7, IVA1;n=24,IVA2; n=7 and IVB;n=2. The median age at diagnosis is 64 years (26-83 years). There have been 2 lymphoma deaths during a median follow-up of 201 months.

CONCLUSIONS: The success of this project will strengthen global connectivity of the CLIC alliance and promote further international collaboration with the aim of providing impactful research and scientific collaboration between experts in cutaneous lymphoma to improve understanding of disease progression and patient care.

¹Scarisbrick JJ et al. CLIC Study of Outcome in Advanced Stages of Mycosis Fungoides & Sézary Syndrome. J Clin Oncology. 2015;33(32):3766-73.

C-02 PROSPECTIVE CUTANEOUS LYMPHOMA INTERNATIONAL STUDY (PROCLIPI) IN EARLY STAGE MYCOSIS FUNGOI-DES

ORAL Scarisbrick JJ^{1*}, Quaglino P², Vermeer M³, Papadavid E⁴, Nikolaou V⁴, Tomasini C², Hodak E⁵, Amitay I⁵, Whittaker S⁶, Morris S⁶, Child F⁶, Bagot M⁷, Ram-Wolff C⁷, Servitje O⁸, Berti E⁹, Alberti-Violetti S⁹, Ortiz-Romero P¹⁰, Gargallo V¹⁰, Stadler R¹¹, Stranzenbach R¹¹, Patsatsi A¹², Koletsa T¹², Jonak C¹³, Knobler R¹³, Porkert S¹³, Mitteldorf C¹⁴, Estrach T¹⁵, Muniesa C¹⁵, Marschalko M¹⁶, Csomor J¹⁶, Cozzio A¹⁷, Guenova E¹⁷, Pimpinelli N¹⁸, Vieri Grandi V¹⁸, Beylot-Barry M¹⁹, Pham-Ledard A¹⁹, Wobser M²⁰, Wehkamp U²¹, Weichenthal M²¹, Dunnill G²², Cowan R²³, Wachsmuth R²⁴, Turner D²⁵, Bates A²⁶, Trautinger F²⁷, Eder J²⁷, Antoniou C⁴, Marinos L⁴, Ekonomidi A⁴, Evison F¹, Kim YH²⁸, Cerroni L²⁹, Kempf W³⁰, Willemze R³

¹University Hospitals Birmingham, Birmingham, UK; ²University of Turin, Torino, Italy; ³Leiden University Medical Centre, Leiden, Netherlands; ⁴Athens University Medical School, Athens, Greece; ⁵Rabin Medical Center, Tel Aviv, Israel; ⁶St Thomas' Hospital, London, UK; ⁷Hospital St Louis, Paris, France; ⁸Hospital Universatari de Bellvitge, Barcelona, Spain; ⁹University of Milano, Milano, Italy; ¹⁰Hospital 12 de Octubre, Madrid, Spain; ¹¹Unit Univ Munster, Minden, Germany; ¹²Aristotle Uni¹versity of Thessaloniki, Thessaloniki, Greece; ¹³Medical University of Vienna, Austria; ¹⁴HELIOS Klinikum Hildesheim GmbH, Hildesheim, Germany; ¹⁵Hospital Clinico, University of Barcelona, Barcelona, Spain; ¹⁶Semmelweis University, Budapest, Hungary; ¹⁷University Hospital Zurich, Zurich, Switzerland; ¹⁸University of Florence, Florence, Italy; ¹⁹CHU Hospital de Bordeaux, Bordeaux, France; ²⁰University Hospital Wuerzburg, Wuerzburg, Germany; ²¹University of Kiel, Kiel, Germany; ²²Bristol Royal Infirmary, Bristol, UK; ²³Christie Hospital, Manchester UK; ²⁴Royal Devon & Exeter Hospital, Exeter, UK; ²⁵Torbay Hospital, Torbay, UK; ²⁶University Hospital Southampton, Southampton, UK; ²⁷University St Poelten, St Poelten, Austria; ²⁸ University of Stanford, Stanford, California, USA; ²⁹Medical University of Graz, Graz, Austria; ³⁰Kempf und pfaltz histologische diagnostik, Zürich, Switzerland

INTRODUCTION: The early-stage PROCLIPI (PROspective Cutaneous Lymphoma Prognostic Index) study registers patients with new diagnoses of mycosis fungoides (MF) stages;IA-IIA.

METHODS: Pre-defined clinical, haematological, radiological, immunohistochemical, genotypic and treatment data is collected on a secure web-based system. The study is co-ordinated through University Hospital Birmingham on behalf of EORTC groups. PRO-CLIPI opened 1/7/2015 with additional non-EU sites opening 2016.

RESULTS: 209 patients (127 male:82 female) are registered from 27 sites indicated in authorship. WHO diagnosis is classical MF;n=170

Scientific Session C: Multinational Collaborative Studies

(81%), folliculotropic MF;n=37 (18%) and pagetoid reticulosis;n=2 (1%). Stage included IA;n=103, IB;n=103 and IIA;n=3. The median age in IA=54yrs and IB=60yrs (p=0.0587). The median MSWAT score was IA;6 (interquartile range:3-8), IB;26 (16-54), IIA;97.5 (67.75-131.25) with no missing data. Blood data was recorded in 72% and 56 patients (37%) had blood involvement classified as B1 (abnormal lymphocytes >5%). Skin biopsy data was recorded in 96%. Most were CD4+ (78.4%). 91 patients (44%) had imaging and 13 patients had lymph nodes 1.5cm or more. 3 patients had a LN biopsy all dermatopathic;N1. 101 patients (48%) had skin clonality tested which was clonal in 60(59%). 62 patients had blood clonality tested and 5 patients (8%) had an identical blood clone. A clinicopathological central review is led by Willemze to agree diagnosis of early-stage MF. 128/209 patients have been reviewed. 95 patients passed the Virtual Review Process. 7 were restaged as advanced-stage, 26 deemed non-diagnostic requiring Real-Time Review, 6 passed and 20 are pending. Virtual Review Pass Rate is therefore 74% rising to 94% following Real-Time Review.

A Federated Biobank (Vermeer) where sites register all tissue samples stored at their site has been a tremendous success with 269 samples registered from 174 patients. So 83% have samples available for future translational projects.

CONCLUSIONS: This is the first prospective study recording pre-defined parameters for skin, blood, lymph nodes and viscera in early-stage MF aiming to identify factors associated with disease progression. Treatments and responses are being recorded to identify best regimes for survival alongside quality of life. Most patients with early-stage disease have a slow disease-course but 25% progress rapidly to advanced-stage and identifying these patients and optimal treatments may improve survival.

C-03 GLOBAL PATTERNS OF CARE IN ADVANCED STAGE MYCOSIS FUNGOIDES/SEZARY SYNDROME: A MULTICENTER RETROSPECTIVE FOLLOW-UP STUDY FROM THE CUTANEOUS LYMPHOMA INTERNATIONAL CONSORTIUM.

ORAL Quaglino P*1, Maule M², Prince HM³, Porcu P⁵, Horwitz S⁶, Duvic M⁷, Talpur R⁷, Vermeer M⁸, Bagot M⁹, Guitart J¹⁰, Papadavid L¹¹, Sanches JA¹², Hodak E¹³, Sugaya M¹⁴, Berti E¹⁵, Ortiz-Romero P¹⁶, Pimpinelli N¹⁷, Servitje O¹⁸, Pileri A¹⁹, Zinzani PL²⁰, Estrach T²¹, Knobler R²², Stadler R²³, Fierro MT¹, Chaganti S⁴, Stevens A⁴, Alberti-Violetti S¹⁵, Amitay-Laish I¹³, Antoniou C¹¹, Combalia A²¹, Fabbro S⁵, Grandi V¹⁷, Jonak C²², Martinez-Escala E¹⁰, Kheterpal M⁶, Kim E²⁴, McCormack C³, Miyashiro D¹², Miyagaki T¹⁴, Muniesa C¹⁸, Nikolaou V¹¹, Ognibene G²⁵, Onida F¹⁵, Porkert S²², Postigo-Llorente C¹⁶, Ram-Wolff C⁹, Rogers K²⁵, Stranzenbach R²³, Rook A²⁴, Willemze R⁸, Hoppe R²⁵, Scarisbrick JJ^{4^}, and Kim YH^{25^}

[^]Julia Scarisbrick and Youn Kim share equal seniorship

¹Dermatologic Clinic, Dept Medical Sciences, University of Torino, Italy: ²Cancer Epidemiology Unit, Dept Medical Sciences, University of Torino, Italy; ³Peter MacCallum Cancer Centre East Melbourne, Australia ⁴University Hospital Birmingham, UK ⁵Ohio State University, Ohio, USA⁶Memorial Sloan-Kettering Cancer Centre, New York, USA ; ⁷MD Anderson Cancer Centre, Houston, USA; ⁸Leiden University Medical Centre, The Netherlands; ⁹Hospital St Louis, Paris, France; ¹⁰Northwestern University, Chicago, USA; ¹¹Athens University Medical School, Greece; ¹²University of Sao Paulo Medical School, Brazil; ¹³Rabin Medical Center, Israel; ¹⁴Faculty of Medicine, University of Tokyo, Japan; ¹⁵University of Milano, Italy; ¹⁶Hospital 12 de Octubre, Madrid, Spain; ¹⁷University of Florence, Italy; ¹⁸Hospital Universitari de Bellvitge, Barcelona, Spain; ¹⁹Dermatologic Clinic, University of Bologna, Italy; ²⁰Seragnoli Institute of Haematology, Bologna, Italy; ²¹Hospital Clinico, University of Barcelona, Spain; ²²Dermatologic Clinic, University of Vienna Medical School, Austria; ²³University Clinic for Dermatology, Venereology, Allergology and Phlebology, Minden, Germany; ²⁴University of Pennsylvania, Philadelphia, PA, USA²⁵Stanford University Medical Centre, California, USA

INTRODUCTION: This is the second study of the Cutaneous Lymphoma International Consortium (CLIC) established with the aim of developing a research network in cutaneous lymphomas and improving the understanding of their clinico- biological characteristics. The objectives were: to analyze treatment distribution according to geographical areas, stage and age of advanced-phase MF/SS patients; to ascertain the association between these parameters and survival.

METHODS: 853 patients stage IIB or higher diagnosed from January 2007 with treatment information retrospectively collected from 21 centres (14 European, 4 USA, 1 Australian, Brazilian and Japanese).

RESULTS: Stage IIB was the most frequent followed by IVA1 and IIIA. Median number of systemic treatment lines per patient were 3 with 38.9% receiving 4 or more. Most commonly used first approaches were extracorporeal photochemotherapy (ECP), bexarotene and phototherapy. As treatment numbers increased, they included poly-chemotherapy, total-skin-electron-beam therapy (TSEBT), histone-deacetylase inhibitors (HDACi), pegylated doxorubicin and allogeneic transplantation. The most frequent sequential therapeutic options were from one systemic immune-modulator to another or from immune-modulators to mono-chemotherapy. Differences in treatment modalities, partly due to difference in drug availability, were found between USA (bexarotene, ECP, HDACi most frequently prescribed independently from stage/age) and non-USA centers (phototherapy, IFN, chlorambucil and gemcitabine). Two survival analyses were carried out. In the first, end-point was death due to any cause and explanatory variables were age, stage and geographical site: age and stage exhibited prognostic significance whilst the geographical site was not associated with mortality. In the second, death and change of therapy were considered as competing risk events and first-line treatment was included among predictors: first-line treatment was selected as independent prognostic variable (p=0.008), both mono- and poly-chemotherapy being associated with higher mortality.

CONCLUSIONS: This unique large multi-centre retrospective study shows the heterogeneity of treatment approaches in advanced MF/SS and their high clinical treatment need. In spite of different availability and use of treatments in USA vs non-USA centres, these were not related to survival outcome, whilst our data reveal that taking stage into account, chemotherapy as first treatment is associated to a higher risk of death and thus other therapeutic options should be preferable as first treatment approach.

Scientific Session C: Multinational Collaborative Studies

C-04 VALIDATION OF CENTRAL PATHOLOGY REVIEW IN ADVANCED-STAGE CUTANEOUS T-CELL LYMPHOMAS, A MULTI-INSTITUTIONAL AND INTERNATIONAL PATHOLOGY PILOT STUDY

ORAL Gru AA*¹, Kim J², Pulitzer M³, Guitart J⁴, Cerroni L⁵, Kempf W⁶, Willemze R⁷, Pawade J⁸, Querfeld C⁹, Schaffer A¹⁰, Pincus L¹¹, Tetzlaff M¹², Duvic M¹², Scarisbrick JJ⁸, Porcu P¹³, Mangold AR¹⁴, Shinohara M¹⁵, Rogers K², Horton B¹, Kim YH²

¹Department of Pathology. Dermatopathology and Hematopathology Sections. University of Virginia, Charlottesville VA. ²Department of Dermatology. Stanford University, Palo Alto, CA. ³Department of Pathology. Memorial Sloan Kettering Cancer Center, New York NY. ⁴Department of Dermatology. Northwestern University. Chicago, IL. ⁵Department of Dermatology. University of Graz, Austria. ⁶Department of Dermatology. University of Zurich, Switzerland. ⁷Department of Dermatology. Leiden University Medical Center, Neatherlands. ⁸University Hospital Birmingham, United Kingdom. ⁹Department of Pathology and Dermatology. City of Hope, Duarte CA. ¹⁰Department of Pathology and Dermatology. Washington University in St. Louis School of Medicine. St. Louis MO. ¹¹Department of Dermatology. University of California San Francisco, San Francisco CA. ¹²Department of Dermatology. MD Anderson Cancer Center. Houston, TX. ¹³Division of Hematology. The Ohio State University. Columbus, OH. ¹⁴Department of Dermatology. Mayo Clinic, Scottsdale AZ. ¹⁵Department of Dermatology. University of Washington, Seattle WA.

INTRODUCTION: Advanced stage mycosis fungoides and Sézary syndrome (AS-MF/SS) is associated with a survival of ~5 years¹. However, high degree of clinico-pathologic heterogeneity exists, with a wide range of outcome within stages. We postulate that such variability is partially linked to the poor reproducibility of the histologic diagnosis of AS-MF/SS. The Cutaneous Lymphoma International Consortium and its PROCLIPI study (Prospective Cutaneous Lymphoma International Prognostic Index) in AS-MF/SS will require minimizing any histopathological inter-observer variability through central pathology review (CPR). The aim of this pilot study is to assess the feasibility and performance of CPR, using digital whole slide scanning, in the characterization of AS-MF/SS (stage IIB or above).

METHODS: A retrospective review of AS-MF/SS cases from 11 different institutions in the US and UK was performed. Two expert panels (AAG, JK, MP, JG and LC, RW, WK, JP) were assembled to evaluate the histologic and immunophenotypic diagnoses of AS-MF/SS. Centralized, whole slide digital imaging was performed using a LEICA scanner. The pathology panelists were provided with the referring diagnosis, immunohistochemistry results, staging information, and clinical description of the lesions. Independent review was done by each of the panelists and entered into the PROCLIPI repository. The referring and panelist diagnosis was compared, and discrepancies were discussed using webinars, in which live slide review was done of the discrepant cases. Consensus was achieved when 2/3 or 3/4 pathologists agreed on the diagnosis. A major discrepancy was considered when a change in the final diagnosis was made, or a discrepancy in the presence of large cell transformation, folliculotropism (FT), granulomatous pattern (GP) or syringotropism (ST) was noted. A minor discrepancy occurred when a different interpretation in Ki67 or CD30 assessment was present.

RESULTS: Preliminary analysis of 31 cases showed a major discrepancy in 29% of cases and a minor discrepancy in 19% of them. Major discrepancies included disagreements in the diagnosis of large cell transformation (44%), and FT/GP/ST (66%). Excellent interobserver agreement (>95%) was achieved upon 'live' revision of the slides in webinars.

CONCLUSIONS: Expert consensus CPR provides a high inter-observer agreement. A similar, optimized, method of evaluation of prognostic biomarkers in AS-MF/SS will be used in PROCLIPI.

¹Scarisbrick JJ et al. CLIC Study of Outcome in Advanced Stages of Mycosis Fungoides & Sézary Syndrome. J Clin Oncology. 2015;33(32):3766-73

Abstracts .

* indicates presenting author

Scientific Session D: Epidemiology & Population Studies

D-01 RELATIVE FREQUENCY, CLINICAL FEATURES, AND SURVIVAL OUTCOMES OF 395 PATIENTS WITH CUTANEOUS LYMPHOMA IN KOREA: A SUBGROUP ANALYSIS PER 10-YEAR PERIOD

ORAL Lee WJ*, Moon IJ, Lee MW

Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

INTRODUCTION: Long-term changes in relative frequency in cutaneous lymphoma (CL) have not been investigated in Asian populations.

METHODS: We investigated the relative frequency, clinical characteristics, and survival outcomes of CL in Korean patients. Moreover, we evaluated the changes in the relative frequency of CL over a 20-year period. After approval was granted from the Institutional Review Board of the Asan Medical Center, the Center's database was searched for all cases of CL that had been confirmed by skin biopsy between January 1994 and December 2013.

RESULTS: The present retrospective cohort study included the total of 395 patients, of whom 289 cases were primary CL and 106 secondary CL, seen at a tertiary referral hospital in Seoul, Korea. Primary CL included T-/NK-cell linage lymphoma (CTCL, 85.1%) and B-cell lineage lymphoma (CBCL, 14.9%). The relative frequency of CBCL increased over time, as shown by a decrease in the CTCL/CBCL ratio from 10.3 in 1994-2003 to 4.5 in 2004-2013. CTCL was more commonly associated with multiple and extensive skin lesions than CBCL. Extranodal NK/T-cell lymphoma (ENKTL) and subcutaneous panniculitis-like T-cell lymphoma (SPTL) were commonly associated with extensive skin lesions. The 5-year overall survival rate for all primary CL patients was 81%.

CONCLUSIONS: Our data show a higher relative frequency of T-/NK-cell lineage Primary CL such as ENKTL and SPTL in Korea compared to the rates reported in Western studies. However, comparison between two 10-year intervals reveals an increasing trend in the incidence of B-cell lineage primary CL and secondary CL in Korea.

D-02 CHARACTERIZATION OF 794 CUTANEOUS LYMPHOMA PATIENTS FROM A SINGLE CENTER IN BRAZIL

ORAL Miyashiro D*, Berg RV, Cury-Martins J, Sotto MN, Halpern I, Zerbini MC, Siqueira SA, Abdo AN, Pereira J, Sanches JA Department of Dermatology, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, Brazil

INTRODUCTION: Cutaneous lymphomas (CL) frequency varies according to geographic location. Our objective was to report CL frequency according to WHO-EORTC classification in a Brazilian cohort.

METHODS: We reviewed clinical, laboratory, and histology data from 786 patients with confirmed CL from a single center institution in Brazil, following criteria proposed by International Society of Cutaneous Lymphomas (ISCL).

RESULTS: From 1989 to 2016, of 1072 patients evaluated at the Cutaneous Lymphomas Clinic, Department of Dermatology, Hospital das Clínicas, University of São Paulo Medical School, there were 794 patients with confirmed diagnosis of CL. Cutaneous T/ NK-cell lymphomas corresponded to 731 patients (92%); cutaneous B-cell lymphomas, to 45 patients (5,6%); eight patients (1%) had CD4+CD56+ hematodermic neoplasm; and ten patients (1,2%) had, besides the CL, other lymphoma or leukemia from a different cell lineage. In the cutaneous T/NK-cell lymphomas group, the diagnoses were: mycosis fungoides in 562 patients (76,9%), Sézary syndrome in 56 (7,6%), cutaneous DC30+ lymphoproliferative disorders in 56 (7,6%), adult T-cell leukemia/lymphoma (ATLL) in 20 (2,7%), primary cutaneous NK/T-cell lymphoma in six (0,8%), subcutaneous panniculitis-like T-cell lymphoma in two (0,3%), small/ medium T-cell lymphoproliferative disorder in two (0,3%), CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma in two (0,3%), and peripheral T-cell lymphoma not otherwise specified in 25 (3,4%). Cutaneous B-cell lymphomas included are: follicle center lymphoma in 16 patients (35,5%); marginal zone B-cell lymphoma in five (11,1%); three cases not distinguishable between follicle center and marginal zone B-cell lymphoma (6,7%); diffuse large B-cell lymphoma, other, in seven (15,5%); diffuse large B-cell lymphoma, leg type, in five (11,1%); diffuse large B-cell lymphoma not specified in two (4,4%); and lymphomatoid granulomatosis with skin involvement in one patient (2,2%).

CONCLUSIONS: We found a higher proportion of cutaneous T-cell lymphomas and a reduced proportion of cutaneous B-cell lymphomas when compared to the United States and Europe. Northeast of Brazil is endemic for HTLV-1, and an increased number of ATLL is observed. These findings highlight the importance of genetic and environmental factors in CL incidence.

Scientific Session D: Epidemiology & Population Studies

D-03 CUTANEOUS T-CELL LYMPHOMA IN SAUDI POPULATION

ORAL Binamer Y*

King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

INTRODUCTION: Cutaneous T-cell lymphoma (CTCL) is uncommon type of non-Hodgkin lymphoma. We are describing the largest series of CTCL patients in Saudi population with emphasize on different clinical presentations.

METHODS: This a retrospective study of patients diagnosed with CTCL at King Faisal Specialist Hospital and Research centre, Riyadh, Saudi Arabia, from 2011-2016.All the clinical data was extrapolated from the medical records and from dermatology database. Age of diagnosis, type of CTCL, morphological variants where all collected.

RESULTS: A total of 135 patients were identified, 6 were in the first decade of life, 15 in the second and 20 in the third. The most common clinical presentation is patch stage. Hypopigmented type is presented in 20% and Poikilodermatous type in 10%. 80% of childhood CTCL was hypopigmented and the youngest patient was at five years of age.

CONCLUSIONS: In our series we are reporting the largest study from Saudi Arabia that describes the clinical presentation of CTCL. What is unique about our data is the prevalence of hypopigmented type is about 20% and the poikilodermatous type is 10%. Four cases of CTCL developed in patients with rheumatoid arthritis.

D-04 PRIMARY CUTANEOUS LYMPHOMA IN ARGENTINA: ANALYSIS OF 416 CASES OF THE PRIMARY CUTANEOUS LYMPHOMA ARGENTINE GROUP

POSTER Abeldaño A*, Enz P, Maskin M, Cervini B, Torres N, Acosta AC, Narbaitz M, Vanzuli S, Fridmanis M, Garcia Pazos ML, Meiss R, Chuit R, Andrade J, on behalf of Cutaneous Lymphoma Argentine Group

Academia Nacional de Medicina, Instituto de Investigaciones epidemiológicas. Hospital Dr. C. Argerich, Hospital Italiano de Bs. A., Hospital de Pediatría Dr. J.P. Garrahan, Hospital Dr. J.M. Ramos Mejía, Hospital Privado de Córdoba, Policlínico Bancario, Hospital Churruca, Psoriahue, Hospital DR. J. Muñiz, Hospital Británico, Hospital Lagomaggiore. Buenos Aires, ARGENTINA

INTRODUCTION: PCL are the second most common type of extranodal non-Hodgkin's lymphoma and mycosis fungoides (MF) is the most frequent cutaneous lymphoma (prevalence 44-59 %) worldwide. Larger differences can be found in the prevalence of rarer entities of lymphoma, depending on the country reporting the cases. To know the epidemiological patterns of PCL in Argentina we conducted a study of PCL cases reported, retrospectively and prospectively over the period January 2010 / December 2015.

METHODS: Case definition was histologically confirmed PCL with appropriate diagnosis and staging. Forms specifically developed to be completed on- line (www.redlinfomacutaneo.org.ar) included: personal data, age, gender, ethnicity, date of onset of symptoms, previous history of: dermatitis, viral infections, malignant neoplasia, exposure to toxic substances and immunosuppression status. Tumor diagnosis (2005 WHO/EORTC classification), histology, molecular biology, and tumor stage.

RESULTS: A total of 416 patients from 21 centers with newly diagnosed cutaneous lymphomas and retrospectively collected data, were reported an included in the analysis. Median age 57 years (range 0-90). M/F ratio=1.35 Previous history of: Inflammatory skin disease 28%, cancer 36% (lymphoma/leukemia=24%). Ninety three % of the cases were CTCL and 7% CBCL. MF and variants were the most common type of PCL (75%) followed by CD30+ PC-LPD (7%), SS (3%) and PC peripheral T-cell lymphoma, unspecified (2%). PC-FCCL was the most frequent type of CBCL (2.9%). Extranodal NK/T-cell lymphoma, nasal type (n=7). Rare disease entities including ATLL (n=2), primary cutaneous CD4+ small/medium TCL (n=1), primary cutaneous CD8+ aggressive epidermotropic cytotoxic TCL (n=5) and subcutaneous panniculitis like TCL (n=5) had a very low incidence. About 75 % of patients were in an early stage, (24 % stage IIB-IVB).

CONCLUSIONS: This study is the first report of the epidemiology of PCL in Argentina and the first multicentre study of Latin America. Compared to other series a higher frequency of MF, a lower frequency of CBCL was found. Further registration and analysis of new cases will be critical for the advancement of knowledge of patterns of PCL subtypes in the country.

D-05 CUTANEOUS MANIFESTATIONS OF ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA IN AN ASIAN POPULATION: CLIN-ICAL CHARACTERISTICS AND CHALLENGES

POSTER Yeo YW*¹, Koh MJ², Koh HY¹, Pang SM¹, Lee HY¹

¹Department of Dermatology, Singapore General Hospital, Singpaore; ²Department of Dermatology, KK Women's and Children's Hospital, Singapore

INTRODUCTION: Angioimmunoblastic T-cell lymphoma (AITL) is a variant of peripheral T-cell lymphomas with cutaneous manifestations reported in up to 50% of cases. Its presentations are myriad and often mistaken for inflammatory dermatosis. Here we review a series of 9 patients seen at an academic medical centre in Singapore aiming to characterize their clinicopathological features and illustrate the spectrum and diagnostic challenges they pose

METHODS: Patients with cutaneous manifestations suspected to be related to AITL seen by the first author at the Department of Dermatology at Singapore General Hospital from January 2012 to December 2015 were included in this series.

RESULTS: 9 patients were identified with a mean age of 69 years(range 51-81)and a slight male predominance of 55%. 5 were of Chinese ethnicity, with 1 Malay, 1 Indian and 2 of other races. Onset of cutaneous manifestations was pre-diagnosis of AITL in 44%(n=4), simultaneous in 33%(n=3) and post-diagnosis in 22%(n=2). In terms of clinical features, 3 patients presented with erythroderma, 3 with a macular or maculopapular exanthem and the remaining 3 with more discrete papules, plaques and nodules.

Scientific Session D: Epidemiology & Population Studies

Not unexpectedly, all 3 presenting with papules, plaques and nodules had lymphomatous infiltrates on histology while only 1 of the remaining 6 patients presenting with either erythroderma or exanthem had definite lymphomatous involvement, suggesting that these manifestations may be either reactive in nature or early in the course of the disease. Of note, one patient with erythroderma had been managed for months for suspected psoriasis refractory to acitretin and methotrexate prior to diagnosis of AITL when she eventually developed lymphadenopathy and systemic symptoms. Skin biopsy showed superficial dermal perivascular infiltrates of CD5 and PD1+ atypical lymphoid cells suggestive of lymphomatous involvement.

CONCLUSIONS: Our study adds to the current literature on cutaneous manifestations of AITL and also highlights that erythroderma, although rarely reported, seems to be over-represented in our series in an Asian population. As such, AITL should also be considered in the differential diagnosis of a new onset erythroderma and enlarged lymph nodes biopsied, particularly if the dermatosis is refractory to treatment.

D-06 PHOTOTHERAPY FOR THE TREATMENT OF MYCOSIS FUNGOIDES IN ASIAN CHILDREN

POSTER Koh MJ*, Chong WS Women's & Children's Hospital and National Skin Center, SINGAPORE

INTRODUCTION: To review a cohort of Asian children with mycosis fungoides treated with phototherapy at a tertiary dermatological center in Singapore.

METHODS: A retrospective analysis of children of Asian descent with a clinical and histological diagnosis of mycosis fungoides treated with phototherapy at the National Skin Centre, Singapore over a period of 5 years from 2004 – 2008.

RESULTS: Eleven patients were identified. Patients were aged between 5 and 13 years, and there were 9 boys and 2 girls. There were 8 Chinese, 2 Indians and 1 Malay patient. The duration from onset of symptoms to time of diagnosis ranged from 4 months to 3 years (mean = 20 months). There were 5 patients with stage 1a disease, 5 patients with stage 1b disease and 1 patient with stage 2a disease. Body surface area involvement ranged from a solitary plaque to 60% involvement. Five patients had lesions of pityriasis lichenoides chronica. None of the patients had systemic involvement. Nine patients were treated with narrow-band ultraviolet B (nbUVB), with 8 patients attaining complete response, defined as more than 75 to 100% clinical clearance. Time to complete response ranged from 2 months to 2 years (mean = 9 months) and after an average of 57 phototherapy sessions (range = 22 – 167). Maximal doses reach ranged from 1300 mJ/cm² to 2497 mJ/cm² (mean = 1920 mJ/cm²). Only 3 patients had sustained remission after follow-up of 1 to 3 years. Five patients had recurrence of lesions after an average of 13.8 months (range = 4 to 36 months). Treatment was well tolerated. One patient was treated with oral psoralen and ultraviolet A (PUVA) therapy in view of plaque stage lesions. However, in view of subsequent ocular contraindications, his parents opted to discontinue treatment. The patient with a solitary plaque was treated with ultraviolet-A1 (UVA-1), achieving partial response after 5 months of medium dose UVA-1 (60J/cm²), 3 months of high-dose UVA-1 (100J/cm²) and 4 months of topical PUVA.

CONCLUSIONS: Mycosis fungoides is an uncommon dermatosis in asian children, with majority of patients having early stage disease. The use of nbUVB is effective and safe in inducing complete response in the majority. However, long-lasting remission occurs in only a third of these patients. Long-term follow-up is essential to monitor for recurrence, which can occur years after remission. Further courses of nbUVB can be instituted for recurrences. We recommend the use of nbUVB as a first line treatment in the management of patch stage mycosis fungoides in asian children. The use of other modalities of phototherapy needs to be further explored.

* indicates presenting author

Abstracts

Scientific Session E. Immunology & Immunopathogenesis

E-01 THE IMMUNE CHECKPOINT RECEPTORS ICOS AND PD1 IN MYCOSIS FUNGOIDES AND SÉZARY SYNDROME: COR-RELATION WITH DISEASE AND OUTCOME.

ORAL Gonzalez BR¹, Song J¹, Weisenburger D¹, Palmer J², Zain J³, Rosen ST^{3,5}, Querfeld C^{*1,3, 4,5} ¹Department of Pathology, ²Department of Hematology/Hematopoietic Cell Transplantation, ³Division of Biostatistics, ⁴Division of Dermatology and ⁴Beckman Research Institute, City of Hope, Duarte, CA, USA

INTRODUCTION: There is accumulating evidence indicating that immune checkpoints play a pivotal role in CTCL. The inducible T cell co-stimulator (ICOS) and programmed cell death PD1 are critical for the regulation of a permissive environment to support the growth of CTCL. The purpose of this project is to study ICOS and PD1 expression in patients with early and advanced stages of mycosis fungoides (MF) and Sézary syndrome (SS) and correlate expression with clinicopathologic features and outcome.

METHODS: Patients were prospectively enrolled and staged according to revised guidelines. mSWAT was performed to assess skin burden. Pathology from 47 skin biopsies were reviewed and immunohistochemistry was performed using a panel of antibodies that included routine markers (CD3, CD4, CD5, CD7, CD8, CD20, CD30, KI67, CD68) and immune checkpoint markers. PD1, PD-L1 and ICOS expression was graded in three different categories by 3 pathologists. The grading was scored using the following criteria: + /rare-scattered (5-15%); ++/numerous (15-30%); +++/high (>30%). Expression level of immune checkpoints was correlated with clinicopathologic features and outcome.

RESULTS: Forty-seven patients with MF/SS were included; 21 patients presented with early stage MF (stages IA-IIA) and 26 patients with advanced MF/SS (stage IIB-IVB). Thirteen patients had large cell transformation (LCT) on histology. High ICOS expression was observed in 10 of 13 patients with LCT and in 5 of 5 patients with SS. Eighteen samples showed high ICOS expression; 12 were from patients with advanced stage MF (stages IIB-IVB), while 6 were from early stage MF (IA-IIA). High expression of PD1 (3+) was also evidenced in 5 of 5 patients with SS but only in 6 of 13 of patients with LCT. Notably, PD-L1 was 3+ in biopsies showing LCT (13 of 13 patients) and/or tumors (9 of 9 patients). High expression correlated with disease burden.

CONCLUSIONS: Immune checkpoints are overexpressed in patients with transformed MF/SS and represent a poor prognostic factor. These preliminary results show that immune checkpoint markers should be considered as complementary immunostains and further investigation is needed to assess the value of these co-regulators for future therapies in MF/SS.

E-02 LACK OF SUPPORT FOR A TH2 ORIGIN OF MYCOSIS FUNGOIDES REVEALED BY RNA SEQUENCING

ORAL Bastidas-Torres AN¹*, Willemze R¹, Vermeer MH¹, Arindrarto W², Tensen CP¹

¹Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands

²Sequence Analysis Support Core, Leiden University Medical Center, Leiden, The Netherlands

INTRODUCTION: Mycosis fungoides (MF) is the most common type of Cutaneous T cell Lymphoma (CTCL), a highly heterogeneous group of extranodal non-Hodgkin Lymphomas that home to the skin. Previous studies claim that MF originates from mature memory CD4+ cells that display a Th2-type cytokine profile. This study aimed at clarifying the origin of MF by comparing the transcriptome of MF tumors with the ones of normal CD4+ $[T_{H}1, T_{H}2, T_{H}17, T_{reg}, T_{EM}, T_{CM}]$ and CD8+ $[naïve, T_{EM}, T_{CM}]$ T-cell subsets. METHODS: Frozen tumor biopsies from MF patients (n=8) were used for RNA extraction. Total RNA was subjected to rRNA de-

METHODS: Frozen tumor biopsies from MF patients (n=8) were used for RNA extraction. Total RNA was subjected to rRNA depletion, library construction and pair-end sequencing on the Illumina HiSeq 2500 platform. Raw data were processed using a customized pipeline which included GSNAP and Cufflinks 2.2.1 for aligning the reads and assembling the transcripts, respectively. Transcriptome data of all T-cell subsets were generated by Ranzani et al. (2015) and obtained from NCBI's GEO database. Additionally, transcriptomes of healthy and psoriatic skin, generated by Di Meglio et al. (2014) and deposited on NCBI's SRA database, were included in the analysis to filter out skin and inflammation-related gene expression. Principal Component Analysis (PCA) and Differential Expression (DE) analysis were performed to assess the degree of similarity between all transcriptomes, and determine differentially expressed genes in MF, respectively.

RESULTS: Th2-type interleukins (IL-4, IL-5, IL-10, IL-13) were found to be either lowly or not expressed in tumor-stage MF. PCA analysis shows that MF has a distinctive expression profile which does not overlap with the ones of the CD4+ and CD8+ T-cell subsets evaluated in this study. DE analysis reveals that histone (e.g. HIST1H1C, HIST1H2BK, HIST1H2BD) and ribosomal proteins (e.g. RPL11, RPL22, RPL27) are among the most up and down-regulated genes in MF, respectively, when compared to normal T-cells. CONCLUSIONS: Contrary to previous reports, our analyses do not support a Th2 origin of MF cells.

Scientific Session E. Immunology & Immunopathogenesis

E-03 INTERLEUKIN-13 IS OVER-EXPRESSED IN CUTANEOUS T-CELL LYMPHOMA CELLS AND REGULATES THEIR PROLIF-ERATION

ORAL Fuschiotti P*, Viragova S, Stolz DB, Geskin LJ University of Pittsburgh School of Medicine; Columbia University

INTRODUCTION: Lack of highly specific markers for malignant lymphocytes prevents early diagnosis of CTCL and timely treatment. The pattern of abnormal Th-2 cytokine expression in CTCL may be responsible for enhanced proliferation of the malignant cells and/or depression of the anti-tumor immune responses in the skin and blood is considered to be of major importance for the pathogenesis of CTCL. We analysed the role of IL-13 and its signalling molecules which are highly expressed by several tumors and act as a growth factor for tumor cells, in CTCL pathogenesis.

METHODS: Immunohistochemistry, confocal immunofluorescence microscopy and flow cytometry were employed to determine expression of IL-13 and its receptors by CTCL skin tumors and leukemic cells. Analysis of tumor cell proliferation after neutralization of IL-13 and its signaling pathways was determined by MTT assay as well as by CFSE staining.

RESULTS: IL-13 and its receptors IL-13Ra1 and IL-13Ra2 are highly expressed in the clinically involved skin of CTCL patients, particularly in advanced-stage disease. Malignant lymphoma cells, identified by the co-expression of CD4 and TOX (thymus high-mobility group box), in the skin and blood of CTCL patients produce IL-13 and express both receptors. Furthermore, tumor cell proliferation was inhibited by neutralization of IL-13 through anti-IL-13 monoclonal antibodies or soluble IL-13Ra2 molecules, and by blocking the

IL-4/IL-13 signalling pathway.

CONCLUSIONS: IL-13 and its signaling mediators are novel molecular markers of CTCL malignancy. Moreover, IL-13 is implicated as a possible autocrine factor for CTCL. We conclude that IL-13 and its signalling molecules represent markers for the early diagnosis of CTCL and potential therapeutic targets for intervention.

E-04 DYSFUNCTIONAL CYTOKINES PRODUCTION INDUCED BY TOLL-LIKE RECEPTORS ACTIVATION IN THE SÉZARY SYNDROME

ORAL Manfrere K*1, Torrealba MP1, Miyashiro DR2, Oliveira LM1, Duarte AJS1, Sanches JA2 Sato MN1

¹ Laboratory of Investigation in Medicine, LIM-56, Department of Dermatology, Tropical Medicine Institute of São Paulo, University of São Paulo Medical School, Brazil. ²Cutaneous Lymphoma Clinic, Department of Dermatology, Hospital das Clínicas, University of São Paulo Medical School, Brazil.

INTRODUCTION: Sézary syndrome (SS) is a rare lymphoma characterized by the clonal expansion of CD4+ T cells with aggressive course. A variety of immunologic abnormalities is founded in cell-mediated immunity of SS as depressed ability to produce the Th1 cytokines. Considering the altered cytokines secretion in SS, activation of innate immunity through activation of Toll-like receptors (TLRs) should be a strategy to potentiate the cytokines production. We evaluated the ability of TLRs (TLR2-TLR9) agonists to induce pro-inflammatory, Th2 cytokines and type I-IFN production by peripheral blood mononuclear cells from SS patients.

METHODS: We enrolled SS patients (n=10, 4 females, 6 males, median of 62-years old) from the Cutaneous Lymphomas Clinic of the Hospital das Clínicas, Department of Dermatology, University of São Paulo Medical School, Brazil (HC/FMUSP), which have not been previously treated, and healthy controls (n= 12, 5 males, 7 females, median age of 55 years), Peripheral blood mononuclear cells were cultured with TLR (TLR2-9) agonists for 48 h and culture supernatants were assessed for cytokines by flow cytometry.

RESULTS: The results showed that SS patients have a highly response of IL-6 and TNF upon TLR2 and TLR4 activation, whereas an impaired response for the agonists of TLR3, TLR5, TLR7, TLR8 and TLR9. IL-10 secretion was induced by both TLR4 and TLR7/8 agonists. Moreover, the IFN- α secretion was restored by TLR9/CpGA and TLR7/TLR8 agonists. The compound able to partially recovered IL-6, TNF and IL-10 as well as type I- IFN production by PBMC from SS patients was CL097, a derivative of the imidazoquinoline compound. The Th2-cytokines, such as IL-4, IL-5 and IL13 induced by TLR8 agonists were barely detected in SS.

Emphasise new and important aspects of the study and conclusions that are drawn from them.

CONCLUSIONS: These findings showed a dysfunctional response to intracellular TLR activation together with a highly response for TLR2/4 agonists which may contribute to the inflammatory profile found in SS patients. Moreover, the TLR7/8 agonist, CL097, suggest to be an adequate adjuvant to restore several types of cytokines in SS.

Scientific Session E. Immunology & Immunopathogenesis

E-05 TIGIT AND HELIOS ARE HIGHLY EXPRESSED ON CD4+ T-CELLS IN SEZARY SYNDROME

ORAL Jariwala N^{*1,2}, Benoit B¹, Kossenkov AV³, Oetjen LK⁴, Whelan TM ^{4,7}, Cornejo CM¹, Takeshita J¹, Kim BS ^{4,5,6,7}, Showe LC³, Wysocka M¹, Rook AH¹

¹Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA ²Drexel University College of Medicine, Philadelphia, PA, USA, ³The Wistar Institute, Philadelphia, PA, USA, ⁴Department of Medicine, Division of Dermatology, Washington University School of Medicine, St. Louis, MO, USA, ⁵Department of Anesthesiology, Washington University School of Medicine, St. Louis, MO, USA, ⁶Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, USA, ⁷The Division of Biology and Biomedical Sciences, Washington University School of Medicine, St. Louis, MO, USA.

INTRODUCTION: Therapeutic options for advanced cutaneous T cell lymphoma (CTCL) are limited and the identification of novel markers may allow for the development of targeted therapies. This study investigated the expression of TIGIT and Helios, two recently described immunosuppression associated molecules, in CD4⁺T cells from CTCL patients.

METHODS: Patients with Sezary syndrome (SS), patients with mycosis fungoides, and healthy volunteers were tested for TIGIT and Helios expression on CD4⁺T-cells by flow cytometry, in association with FCRL3, FoxP3, CD25, CD26, and TCRVβ clones. Real Time Quantitative PCR was used to assess TIGIT, Helios, and FCRL3 mRNA expression in the skin. IFN-γ, IL-10, IL-2 intracellular production assessed by flow cytometry following PMA/ionomycin stimulation. Clinical differences among patients with high and low Helios and TIGIT were analyzed, in terms of blood tumor burden, advanced age, high LDH, and male gender (factors previously linked to poor prognosis).

RESULTS: Increased expression of both TIGIT and Helios was observed on CD4⁺ T cells from SS patients. TIGIT was primarily expressed on CD26⁻ TCRVB⁺CD4⁺ T cells and its expression correlated with the expression of FCRL3, CD164, and a poor prognosis. TIGIT⁺CD4⁺T cells demonstrated diminished production of IFN- γ and IL-2 compared to TIGIT⁻ CD4⁺T cells. Unlike TIGIT, elevated Helios expression was demonstrated on both CD26⁻ and CD26⁺ CD4⁺T cells from SS patients with a wide range of circulating tumor burdens. Helios expression correlated only with the expression of CD164. Significant expression of TIGIT, Helios, and FCRL3 mRNA was also demonstrated in the skin of CTCL patients.

CONCLUSIONS: Our data imply that increased Helios, and, particularly TIGIT expression in SS may play a role in attenuating the immune response, providing insight into the immunosuppressive nature of the disease, and suggests another potential means of targeted therapy.

E-06 MYCOSIS FUNGOIDES: NEW ISSUES FROM MICROENVIRONMENT

ORAL Pileri A*1,3*, Agostinelli C², Grandi V³, Delfino C³, Patrizi A¹, Pimpinelli N³

¹Dermatology Unit, Department Of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Italy; ²Haematopathology Unit, Department Of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Italy; ³Departement of Surgery and Translational Medicine, Division Dermatology, University of Florence, Italy.

INTRODUCTION: Mycosis fungoides (MF) shows a clinical outcome stage-related, with early stages showing an indolent behaviour and progressively more aggressive disease in advanced ones. Tumour immune escape response mechanisms are well-known strategies involved in tumour growth and metastasis of different neoplasms. However, little is known about that in CTCL. Our aim was to investigate Langerhans cells (LC), plasmocytoid dendritic cells (pDCs) as well as myeloid derived dendritic cells suppressor (MDSCs) distribution in early and advanced MF lesions.

METHODS: Forty-six patients in various stages, corresponding to 65 MF biopsies from databases of Turin, Bologna and Florence Lymphoma Units, were retrieved. Langherin, CD303 and Arginase expression were analysed.

RESULTS: Our data show a decrease in Langherin expression from patch/plaque lesions to tumour stage (p-value 0.03), and in addition an increase in CD303 and Arginase expression (p-value <0.01). Interestingly, comparing tumor stage (stage IIB) to erythrodermic patients (stage III) we observed an increase in Langherin expression (p-value: .02), while a decrease was observed comparing stage III to IV (p-value: .02)

CONCLUSIONS: The LC decrease from stage I to IIB could be related to an empowerment of the MF tumor immune escape response mechanism, leading to a decrease in immune system activation because of the production of tolerogenic cytokines. The changes in Langherin expression comparing stage III to IIB and IV could rise the question as to whether erythrodermic CTCL could feature different pathobiology, different tumour immune escape response mechanisms, and should be regarded as a prognostically distinct category. Albeit other groups already reported an increased number of pDCs in MF lesions, for the first time we provide evidence of a significant increase from early to advanced lesions, questioning if the pDC increase could be related to an accumulation of immature pDC, eventually leading to immunosuppression. We analysed MDSCs distribution in MF and observed an increase in Arginase expression from stage I to IIB. Such a change suggests that MDSCs could play a role in MF progression, decreasing the anti-tumour immune response and therefore being regarded as a worse prognostic marker. In conclusion, we have observed a different recruitment pathway of LCs, pDCs and MDSCs among MF stages, especially between stages I and IIB, suggesting that microenvironmental changes could play a role in MF progression, thus opening up new scenarios in MF therapy.

Scientific Session E. Immunology & Immunopathogenesis

E-07 IMPAIRED SECRETION OF CXCL9/MIG AND CXCL10/IP-10 IN SÉZARY SYNDROME

ORAL Torrealba MP*1, Manfrere K1, Miyashiro DR2, Oliveira LM1, Sato MN1, Sanches JA2

¹ Laboratory of Investigation in Medicine, LIM-56, Department of Dermatology, Tropical Medicine Institute of São Paulo, University of São Paulo Medical School, Brazil. ²Cutaneous Lymphoma Clinic, Department of Dermatology, Hospital das Clínicas, University of São Paulo Medical School, Brazil.

INTRODUCTION: Sézary syndrome (SS) is a leukemic variant of cutaneous T-cell lymphoma, with clonal proliferation of neoplastic CD4+T-cells. Cell migration and activation driven by interaction between chemokines and chemokine receptors play a pivotal role in the pathogenesis of various neoplasms and inflammatory disorders. The aim of this study was to investigate the profile of chemokine secretion induced by Toll-like receptors (TLR) agonists in peripheral blood mononuclear cells (PBMC) from SS patients. Moreover, we verified the effect of IFN- γ priming in the secretion of CXCL9/MIG and CXCL10/IP10 (IFN- γ -inducible-chemokines) in PBMC and TCD4+CD158k+ malignant T-cells.

METHODS: We enrolled 11 SS patients (61 years-old \pm 7.8) without previous treatment, and three SS patients under treatment from the Cutaneous Lymphoma Clinic, Department of Dermatology, Hospital de Clínicas, University of São Paulo Medical School, Brazil. Thirteen healthy donors (HD) were enrolled as controls (55 years-old \pm 5)

RESULTS: High levels of circulating CXCL9 and CXCL10 were observed in the serum from SS patient. Besides that, in PBMC culture supernatants, at baseline and after stimulation, levels of CXCL9 and CXCL10 were higher in HD than in SS. On the other hand, CXCL10 secretion was induced only by TLR9 agonist in SS patients, and by TLR9 and TLR7/8 agonists in HD. Moreover, the patient's therapy didn't change the profile of CXCL9 and CXCL10 secretion by PBMC in the three SS patients evaluated. In these patients, priming with IFN- γ restored CXCL9 and CXCL10 secretion by PBMC at the similar levels of HD subjects, except for one patient, who seems refractory to IFN- γ priming. The source of CXCL9 and CXCL10 observed in sera is probably due to monocytes, since the isolated CD4+ T-cells barely secrete these chemokines. IFN- γ priming was more effective in CXCL10 secretion by TCD4+CD158k-than TCD4+CD158k+ malignant cells.

CONCLUSIONS: We found that PBMC from SS patients have decreased CXCL9 and CXCL10 secretion capacity when compared to HD. In SS patients, IFN-γ priming reversed this chemokine secretion impairment in PBMC, but not in TCD4+CD158k+ cells.

E-08 INEFFECTIVE ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY IN PATIENTS WITH LATE STAGE CUTANEOUS T CELL LYMPHOMA

ORAL Chang YT¹, Ziegler M¹, Ignatova D¹, Ivanov P², Profanter R², Kerl K¹, Dummer R¹, French L¹, Cozzio A⁴, Misailovic S^{2,3}, Hoetzenecker W⁴, Vechev M², Guenova E^{*1,4}

¹Department of Dermatology, University Hospital of Zürich, University of Zürich, Switzerland; ²Software Reliability Lab, Department of Computer Science, ETH Zürich, Switzerland; ³Computer Science Department Department, University of Illinois at Urbana-Champaign, USA; ⁴Department of Dermatology, Kantonspital St. Gallen & University of Zürich, Switzerland

INTRODUCTION: Targeted therapies and immune modulators are currently changing our understanding for the treatment of solid tumors, and promise to open a new perspective in the management of cutaneous T-cell lymphoma (CTCL) as well. The mechanisms of action of therapeutic antibodies in vivo is not fully elucidated in all cases, antibody-dependent cellular cytotoxicity (ADCC) mediated by natural killer (NK) cells often being presumed to be a key mode of action. However, since progressive impairment of cellular immunity is a hallmark of CTCL, we questioned the fact that patients with late stage CTCL will still be in a possession of fully functional ADCC.

METHODS: NK cells were isolated from patients with MF stage I-IV, Sézary Syndrom (SS) patients and healthy individuals. An aCel-Ia-TOX GAPDH assay was used to detect the amount of endogenous glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and the level of ADCC in each individual patient.

RESULTS: In vitro ADCC in patients with MF stage I was comparable to that of healthy individuals, but severely abrogated in all MF Stage IV and SS patients included in the study. The percentage of NK cells in the blood of CTCL patients was within normal limits. Trogocytosis, a mechanism of cellular communication that can hamper ADCC by cleaving the surface of the tumor cells from the targeted molecule, seemed not to play an essential role in CTCL. However, overexpression of MHC I on the malignant tumor cells in CTCL was important factor in helping tumor cells escape NK-cell activity and MHC I blockade could restore impaired ADCC.

CONCLUSIONS: Impaired ADCC may pose some problems when choosing a targeted drug therapy for the treatment of late stage CTCL. Understanding of the immunological mechanisms behind it will help improve NK cell activity in CTCL patients and overcome resistance to treatment.

Scientific Session E. Immunology & Immunopathogenesis

E-09 CHARACTERIZATION OF THE TUMOR MICROENVIRONMENT IN PRIMARY CUTANEOUS CD30-POSITIVE LYMPHOP-ROLIFERATIVE DISORDERS: A PREDOMINANCE OF CD163-POSITIVE M2 MACROPHAGES

ORAL Kempf W^{*1}, De Souza A^{1,2}, Burghart DR¹, Berisha A¹

¹Kempf and Pfaltz Histologische Diagnostik, Zürich, Switzerland, ²Department of Dermatology, Harvard Medical School, Boston, MA

INTRODUCTION: The tumor microenvironment is essential for tumor survival, growth and progression. There are only a few studies on the tumor microenvironment in cutaneous CD30-positive lymphoproliferative disorders.

METHODS: We assessed the composition of the tumor microenvironment using immunohistochemistry studies in skin biopsies from cases diagnosed with lymphomatoid papulosis (LyP: 18 specimens), primary cutaneous anaplastic large-cell lymphoma (PC-ALCL: 8 specimens), and reactive diseases harboring CD30-positive cells (18 specimens).

RESULTS: The predominant cells present in LyP and PC-ALCL were CD163+ M2 macrophages (44.7%, 35%), followed by CD8+ tumor infiltrating lymphocytes (11%, 15%), FOXP3+ T-regulatory cells (9%, 4.5%) and programmed cell death 1(PD-1)+ lymphocytes (2.2%, 6.8%). In contrast, CD30-positive reactive inflammatory and infectious disorders were characterized by higher numbers of CD123+ plasmacytoid dendritic cells (6.3%) when compared to LyP (1%), and PC-ALCL (1.1%).

CONCLUSIONS: Key differences exist between the microenvironment of CD30-positive lymphoproliferative disorders and reactive conditions harboring CD30-positive lymphocytes. The high number of tumor associated macrophages, and the close vicinity of these immune cells to the CD30-positive tumor cells might suggest that tumor associated macrophages have direct influence on tumorigenesis in LyP and ALCL. Therefore, modulation of M2 macrophages may represent a new therapeutic strategy in cutaneous CD30-positive lymphoproliferative disorders.

E-10 IL-10 IS A BIOMARKER OF ADVANCED MYCOSIS FUNGOIDES AND IS REQUIRED FOR MAXIMAL TUMOR FORMA-TION IN A MURINE MODEL OF CTCL

ORAL Wu X*1, Youwen Z², Hwang S¹

¹Dermatology, University of California Davis, Sacramento, CA, USA ²Dermatology and Skin Sciences, University of British Columbia, Vancouver, BC, Canada

INTRODUCTION: IL-10 is a potent immunoregulatory cytokine with pleotropic functions that has been reported to be increased in the lesional skin of patients with advanced stages of cutaneous T cell lymphoma (CTCL). It is unclear, however, if IL-10 is a biomarker of advanced disease or if it is required for tumorigenesis.

METHODS: We used PCR array to examine the inflammatory cytokine profiles in skin samples of mycosis fungoides (the most common type of CTCL) patient. We also examined the expression levels of IL-10 and related immune regulators in a murine model of CTCL which we previously reported. We compared tumor development of implanted MBL2 tumors in IL-10 gene KO (IL-10KO) mice vs. wild-type (WT) mice. Lastly, we used antibody-mediated blockade for IL-10 signalling pathway in order to consolidate the role of IL-10 pathway in CTCL tumor growth.

RESULTS: We confirmed that IL-10 expression was increased (~6 fold compared to normal skin) in the skin samples of mycosis fungoides and that IL-10 mRNA level was 2-3 fold higher in plaque than in patch stage mycosis fungoides (p=0.0428). In murine model, we showed that IL-10 was upregulated in tumors that developed in skin of mice. Notably, tumors arising in IL-10KO mice were 50% smaller (n=15, p=0.0026) than those of control mice. Immunostaining revealed a significant decrease of 9.7-fold fewer F4/80+ macrophages, the major producer for IL-10, in IL-10KO vs. WT tumors (p=0.048). When administering neutralizing antibody for IL-10R in wild type mice, the ear tumor thickness decreased 40% (p=0.04) in treated mice compared to controls. Interestingly, when we administered anti-IL-10R in IL-10KO mice, ear tumor thickness decreased an additional 43.5% (p=0.003), which suggesting that the host-produced IL-10 accounts part of the tumor-stimulating activity of this cytokine.

CONCLUSIONS: Our data confirm that IL-10 is upregulated in the skin of advanced CTCL patients. IL-10 is required for maximal tumor development in mouse model and may contribute to the accumulation of macrophages in tumor environment. Thus, targeting of IL-10 pathways, potentially with neutralizing antibodies to IL-10 or its receptor, should be considered for treating advanced CTCL in the clinic.

Scientific Session E. Immunology & Immunopathogenesis

E-11 SIGNIFICANCE OF IL-31 EXPRESSION IN SKIN AND IN SERUM IN PATHOGENESIS OF CTCLS AND IN PATHOMECH-ANISM OF ACCOMPANYING PRURITUS

POSTER Olszewska B*, Żawrocki A, Malek M, Gleń J, Lange M, Sokołowska-Wojdyło M, Nowicki R Clinic of Dermatology, Venerology and Allergology, Medical University of Gdańsk, Poland

INTRODUCTION: Primary cutaneous T-cell lymphoma (CTCL) is a chronic disease accompanied by persistent pruritus which responds poorly to antihistamines and therefore significantly reduces quality of life. Moreover its pathogenesis remains unclear. Due to conflicting reports on the role of IL-31 in pathogenesis of pruritus accompaning CTCL, we ought to develop the subject of IL-31 in CTCL. Thie aim of this study was to investigate IL-31 expression in the skin and in the serum of CTCL patients.

METHODS: The study group included 51 patients with CTCL and 40 healthy volunteers. Pruritus severity was evaluated with the Visual Analogue Scale (VAS) and Numeric Raating Scale (NRS). Expression of IL-31 was evaluated in formalin-fixed paraffin-embedded biopsy specimens from CTCL patients and healthy individuals by means of immunohistochemical staining. We used Malek et al (from our Deprtment) research results including serum IL-31 levels in CTCL patients, which were determined by the enzyme- linked immunosorbent assay methodology.

RESULTS: Pruritus affected 64,7% of patients with CTCL. The mean \pm SD pruritus severity score for CTCL patients with pruritus according to NRS was 4.5 \pm 2.3 and VAS was 4.4 \pm 2,5. IL-31 was elevated in the epidermis and dermal infiltrate in the CTCL patients. IL-31 expression was significantly elevated in skin from CTCL patients compared to healthy skin from control group (p<0.001). We investigated the correlation between the IL-31 skin levels, IL-31 serum levels, pruritus and stage of the disease. Based on the pre-liminary results of our research, it seems that IL-31 is involved in pathogenesis of CTCL.

CONCLUSIONS: We have demonstrated that IL-31 is overexpressed in the skin of CTCL patients. These results indicate IL-31 involvement in pathogenesis of CTCL.

E-12 DISSECTING THE IMMUNE LANDSCAPE OF MYCOSIS FUNGOIDES

POSTER Murray DJ*1, Yoo J², Eldershaw S¹, Pearce H¹, Moss PAH¹, Scarisbrick JJ²

¹Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK; ²Department of Dermatology, University Hospitals Birmingham, Birmingham, UK

INTRODUCTION: Understanding the pattern of immune checkpoint expression in mycosis fungoides (MF) will be important for interpreting the potential clinical utility of antibody-mediated checkpoint inhibition. MF presents a challenge in this regard in that CD4+ T cells are believed to be an important component of the tumor-specific immune response and yet this phenotype is shared by the tumor cell. We have utilized staining with T cell receptor (TCR) V-beta specific antibodies to discriminate between tumor and tumor-infiltrating lymphocytes (TILs) and allow an accurate phenotypic profile of checkpoint protein expression.

METHODS: Seven patients with patch (n=2), plaque (n=2) or tumor (n=3) mycosis fungoides had a 6mm punch biopsy and paired peripheral blood taken. Skin was digested and a TCR V-beta clonogram performed to determine the V-beta family expression of the tumor. Both skin and blood were analyzed directly, using multi-parameter flow cytometry to separate peripheral blood CD4 and CD8 T cell subsets, CD4 and CD8 TILs and tumor cell populations. These populations were compared for expression of PD-1, PD-L1 & PD-L2, as well as other immune checkpoint markers.

RESULTS: Utilizing TCRV-beta-specific antibodies directly on uncultured cells successfully discriminated between CD4 tumor and TIL cells in 5 out of the 7 samples. These two populations demonstrated distinct phenotypes, with tumor cells having a higher side and forward scatter on flow cytometry. PD-1 expression was high on CD4+ and CD8+ TILs and was markedly upregulated on tumor cells. The expression of the two PD-1 ligands (PD-L1 and PD-L2) was assessed on these populations and demonstrated interesting patterns of variation between samples.

CONCLUSIONS: The method of using a TCRV-beta-specific antibody directly on macerated tissue allows the phenotyping of tumor and TIL populations in MF. TILs in MF demonstrate the typical pattern of T cell 'exhaustion' that has been observed in other forms of cancer. Tumor cell PD-1 expression was variable, but could be very high and may reflect a pattern of cellular activation. This information should prove of value in guiding the appropriate introduction of checkpoint blockade. * indicates presenting author

Abstracts

Scientific Session F. Biomarkers

F-01 INCREASED SOLUBLE CD226 IN SERA OF PATIENTS WITH CUTANEOUS T-CELL LYMPHOMA MEDIATING CYTOTOXIC ACTIVITY AGAINST TUMOR CELLS VIA CD155

ORAL Takahashi N*¹, Sugaya M¹, Suga H¹, Oka T¹, Kawaguchi M¹, Miyagaki T¹, Fujita H¹, Inozume T², Sato S¹ ¹Department of Dermatology, University of Tokyo Graduate School of Medicine, Tokyo, Japan. ²Department of Dermatology, University of Yamanashi, Kofu, Japan.

INTRODUCTION: CD155, which is expressed in various types of cancer, can mediate activation of NK and T cells via CD226 and their inhibition via T cell immune receptor with Ig and ITIM domains (TIGIT). In this study, we investigated expression and function of CD155, CD226, and TIGIT in cutaneous T-cell lymphoma (CTCL).

METHODS: Skin samples were collected from 19 patients with CTCL and eight healthy control subjects and quantitative RT-PCR was performed. CD226 expression on the surface of NK cells and CD8⁺ cells were examined by flowcytometry in peripheral blood from 18 patients with CTCL and 11 healthy subjects. Serum levels of CD226 were measured in 41 CTCL patients and 20 healthy control subjects. To investigate the effect of soluble CD226 in CTCL patients, we examined cytotoxic activity using recombinant CD226 and CTCL cell lines (SeAX cells and HH cells) *in vitro*.

RESULTS: CD155 was strongly expressed on CTCL tumor cells. CD155 mRNA expression levels were increased with disease progression in CTCL lesional skin, which significantly correlated with TIGIT and CCL17 expression levels. CD226 expression on NK cells and CD8⁺ cells in peripheral blood was decreased, while serum CD226 levels were elevated in CTCL patients, suggesting that soluble CD226 in sera was generated by shedding of its membrane form. More interestingly, recombinant CD226 itself showed cytotoxic activity against CD155-expressing CTCL tumor cells *in vitro*.

CONCLUSIONS: Our study has suggested that soluble CD226 elevated in sera of CTCL patients would be important for tumor immunity by interacting with CD155 on tumor cells.

F-02 EVALUATION OF VALIDATED DNA METHYLATION BIOMARKERS IN EARLY SÉZARY SYNDROME PATIENTS

ORAL Zoutman WH*1, Najidh S1, Bagot M2, Michel L2, Tensen CP1, Vermeer MH1

¹Dept. of Dermatology, Leiden University Medical Center, Leiden, Netherlands; ²Dept. of Dermatology. Hôpital St. Louis, Paris, France

INTRODUCTION: Sézary syndrome (SS) is an aggressive type of cutaneous T-cell lymphoma with a poor prognosis. Diagnosing Sézary syndrome can be challenging especially in early stages of disease. In a recent study we show that aberrant promoter methylation of *PROM1*, *GOS2*, *CMTM2*, *C2orf40*, *PAM*, *GNMT* and *NEXN* is frequently observed in Sézary syndrome but is not found in benign erythrodermic patients with a diagnostic sensitivity of 80-100% and specificity of 100%. In this study we evaluated if promoter methylation status of these seven genes could be helpful in diagnosing patients with early stages of disease and low tumor burden in peripheral blood (B1).

METHODS: Peripheral blood was drawn from 22 early SS patients at stage T4NxMxB0 and/or T4NxMxB1. DNA was extracted from CD4+ enriched T cells and subjected to methylation-specific melting curve analysis (MS-MCA) in order to evaluate methylation status. All patients had progressive disease and fulfilled WHO criteria for Sézary syndrome during follow up.

RESULTS: In 73% of early SS patient samples one or more of the seven selected biomarkers was hypermethylated. Aberrant hypermethylation of at least one of the seven selected genes was observed in 80% of T4NxMxB1 patients and 40% of T4NxMxB0 patients. The most frequently hypermethylated markers were *G0S2* and *PAM* (both 73%).

CONCLUSIONS: These data show that the methylation status of a panel of 7 biomarkers (*PROM1*, *G0S2*, *CMTM2*, *C2orf40*, *PAM*, *GNMT* and *NEXN*) can be helpful in early diagnosis of SS which can have beneficial effects on treatment and quality of life.

F-03 VARIABILITY IN CD30 AND OTHER BIOMARKER EXPRESSION LEVELS IN MYCOSIS FUNGOIDES/SÉZARY SYN-DROME (MF/SS): CHALLENGES IN TISSUE BIOMARKER INTERPRETATION

ORAL Rahbar Z^{*1}, Li S¹, Kim J¹, Almazan TH¹, Sundram U¹, Kim YH¹ ¹Stanford Cancer Institute, Stanford, CA

INTRODUCTION: Characterizing tissue malignant cells and the microenvironment using immunohistochemistry (IHC) is essential for exploring biomarkers of new targeted agents. In MF/SS, biomarker interpretation may be challenging given the heterogeneity of skin lesions. Utilizing samples collected in our phase II study of brentuximab vedotin in MF/SS, we evaluated the variability in IHC-based assessment of tissue markers.

METHODS: At screening, two or more pairs of side-by-side biopsies of different sites and/or lesion types (patch, plaque, tumor) were collected. IHC was graded as the percentage of total mononuclear cell infiltrate. Intra-class correlation coefficients (ICC) estimated biomarker variability in the same lesion ("intralesional") and between two different lesions in the same patient ("interlesional"). The range of variability in biomarkers across all patients was evaluated by calculating the Δ (maximum-minimum) of each marker for each patient.

RESULTS: 111 skin biopsies from 32 patients were studied. Stage >IIB, 88%; LCT, 69%. Intra-rater reliability was high (ICC=0.89) upon re-rating of slides. 6/32 (19%) patients demonstrated maximum CD30 expression in a lesion other than the most clinically advanced lesion. The variability in biomarker expression is summarized in Table 1. Despite variability among types of lesions, increasing trends in expression were detected (median Δ of patch, plaque, tumor) for CD30 (1, 4, 11), CD20 (1, 5, 10), CD163 (10,

* indicates presenting author

Scientific Session F. Biomarkers

20, 20), Ki67 (5, 10, 20), TIA1 (1, 5, 8) and possible decreasing trends for CD8 (18, 15, 15), FoxP3 (0, 10, 4) and langerin (4, 3, 1). CONCLUSIONS: Notable intra-patient variability in skin IHC features was observed in MF/SS. Multiple biopsies may decrease sampling error and interpretative bias, and conclusions based on IHC assessment should be derived cautiously. The clinical significance and applicability of observed trends or variability needs further studies.

Table-1. Variability in biomarkers			
IHC	Intralesional ICC	Interlesional ICC	Δ [max-min], %, median (range), all patients
CD8	0.61	0.53	17 (0-55)
CD25	0.47	0.54	30 (4-70)
CD30	0.63	0.45	7 (0-95)
CD163	0.22	0.43	20 (0-60)
FoxP3	0.54	0.57	10 (0-35)
Ki67	0.67	0.42	18 (0-70)

F-04 CXCL13 AND BOB1 EXPRESSION IN INITIAL BIOPSIES OF MYCOSIS FUNGOIDES WITH STABLE EARLY STAGE AND LATER TUMOR STAGE DISEASE

ORAL Wehkamp U^{1*}, Oschlies I², Kohler C³, Weichenthal M¹, Klapper W²

¹Department of Dermatology, University Hospital Schleswig-Holstein, Campus Kiel; ²Institute of Pathology, Hematopathology Section, University Hospital Schleswig-Holstein, Campus Kiel; ³Institute of Functional Genomics, Statistical Bioinformatics Department, University of Regensburg, Germany

INTRODUCTION: Mycosis fungoides (MF) is the most common cutaneous T-cell- lymphoma (CTCL) accounting for approximately 50% of all CTCL with a wide range of initial disease presentation and evolution over time. However, in early disease stages biomarkers as indicators of a later progression have not yet been identified.

METHODS: Of 173 patients with confirmed MF, treated at the Department of Dermatology, University Kiel, (1995-2015), 17 patients with stable disease MF ('MF stable') defined as T1aN0M0B0 over a period of more than 5 years were identified and compared to 20 patients with later evolution to tumor-stage MF ('MF tumor'). We investigated the initial diagnostic specimen of these patients by gene expression profiling for 770 different genes related to immunological mechanisms and cancer (Nanostring/nCounter) with a protocol optimized for formalin fixed paraffin embedded tissue. For the validation of differential gene expression, immunohistochemistry was performed for selected markers, i.e. CXCL13 and BOB1.

RESULTS: The gene expression profiling identified 36 genes with a statistically significant differential expression between 'MF stable' and 'MF tumor' specimen ($p \le 0,05$). Within these, we observed a higher expression of several genes pointing towards a follicular T-helper phenotype in samples of patients with later tumor-stage development, among them CXCL13 and IL21. Additionally, in these samples higher B-cell marker gene expression was detected (CD79A). Semiquantitative analysis of immunohistochemistry for BOB1 and CXCL13 in fact confirmed a higher number of positive cells in lesions of 'MF tumor' compared to 'MF stable'.

CONCLUSIONS: We identified genes in initial biopsies of MF that differ between diseases with a long stable course and those with progression to a tumor stage. Interestingly, differential gene expression in samples of patients with later progression points towards a follicular T-helper cell phenotype. For Bob1, which is basically a B-cell specific transcriptional coactivator, a role in the memory function of CD4+ cells has been described recently. Further exploration is required to determine, whether higher expression in early disease stages might be a relevant contributive factor to tumor development in MF patients. The present data provides insights into pathogenesis and might display future perspectives for routine diagnostic biomarkers.

Scientific Session F. Biomarkers

F-05 USEFULNESS OF KIR3DL2 TO DIAGNOSE, FOLLOW-UP AND MANAGE THE TREATMENT OF SÉZARY SYNDROME PATIENTS

ORAL Hurabielle C*^{1,2}, Thonnart N^{2,3}, Ram-Wolff C^{1,2,3}, Sicard H⁴, Bensussan A^{2,3#}, Bagot M^{1,2,3#}, Marie-Cardine A^{1,2,3#} ¹Department of Dermatology, Saint-Louis Hospital, AP-HP, Paris, France; ²INSERM U976, Saint-Louis Hospital, Paris, France; ³Paris Diderot University, Sorbonne Paris Cité, Paris, France; ⁴Innate Pharma, Marseille, France; [#]These authors contributed equally to the work.

INTRODUCTION: KIR3DL2 is a recently discovered marker of the malignant clonal cell population in Sézary Syndrome (SS). We intended to evaluate the expression of KIR3DL2 on blood T-cells as a diagnostic, prognostic and follow-up marker of SS. METHODS: 64 patients diagnosed with SS were included in this monocentric study. We collected the percentage of KIR3DL2+ cells among CD3+ T-cells, obtained by flow cytometry, and other classical diagnostic criteria for SS at diagnosis and during the follow-up. RESULTS: KIR3DL2 was the most sensitive diagnostic factor for SS when compared to the classical diagnostic factors. Indeed 87.5% of the patients had abnormal percentages (>5%) of KIR3DL2-positive cells among their T-cells population at diagnosis while 79.5% showed a Sézary cell count >1,000/mm3 and 73.4% a CD4/CD8 ratio >10. Univariate and multivariate analyses established that an eosinophil cell count >700/mm3 and a percentage of KIR3DL2+ cells within the CD3+ T-cells >85% at diagnosis were associated with a significant reduced disease-specific survival. In addition, KIR3DL2 immunostaining allowed the assessment of treatment efficiency and specificity towards tumour cells, the detection of the residual disease following treatment, and the occurrence of relapse, even though patients experienced complete remission and/or undetectable circulating Sézary cells by cytomorphologic analysis. CONCLUSIONS: We show that KIR3DL2 expression is the most sensitive diagnostic criteria of SS as compared with all other available biological criteria. It also represents the main independent prognostic factor for SS-specific death and the most relevant feature for the follow-up of SS, showing the invasion of the functional lymphocytes pool by tumour Sézary cells. KIR3DL2 therefore represents a valuable tool for a routine use as a clinical parameter at diagnosis, prognosis and during patients follow-up. Beside its use as a specific marker for CTCL malignant T-cell clone, KIR3DL2 may also represent an attractive therapeutic target for this disease. In this regard, promising pre-clinical results were obtained by using an anti-KIR3DL2 antibody able to promote both antibody-dependent cell cytotoxicity and phagocytosis, leading to a specific depletion of the tumour cells. Such approach sounds promising as minimal side effects are expected from the antibody mode of action.

F-06 C-MET IS OVEREXPRESSED IN CUTANEOUS T-CELL LYMPHOMA AND REPRESENTS A POTENTIAL THERAPEUTIC TARGET

ORAL Laturnus M¹, Haider A², Lenze D³, Möbs M³, Hummel M³, Mathas S⁴, Assaf C^{1,2*}

¹Department of Dermatology, HELIOS Klinikum Krefeld, Krefeld, Germany, ²Department of Dermatology, Charité – Universitaetsmedizin Berlin, Berlin, Germany; ³Institute of Pathology, Charité – Universitaetsmedizin Berlin, Berlin, Germany; ⁴Department of Hematology and Oncology, Charité – Universitaetsmedizin Berlin, Berlin, Germany

INTRODUCTION: Despite significant progress made in the identification of novel genes and pathways involved in the pathogenesis of cutaneous lymphoma, the therapeutic value of these findings is still elusive, and there remains a particular need for treatments of patients with advanced stage cutaneous lymphoma. The c-MET-receptor is a physiological membranous tyrosine-kinase-protein on endothelial and epithelial cells, which can be overexpressed in many solid and hematological malignancies. The c-MET-activation is followed by numerous intracellular pathways, as for example the RAS/RAF/MEK/MAPK- or the PI3K/AKT-signaling cascades, which are playing an important role in cell-proliferation, -survival and –mobility in cutaneous T cell lymphoma.

METHODS: To detect the genetic and protein expression status of c-MET - next generation sequencing, gene expression analyses, real-time PCR, western Blot, FISH and immunohistochemistry were done on cell lines and primary tumor material from patients having CTCL. c-Met overexpression was correlated to the clinical stage of CTCL patients. In addition functional investigations as inhibitory analyses using a c-MET inhibitor with subsequent tests on proliferation and apoptosis were done.

RESULTS: c-MET overexpression could be demonstrated in cell lines and CTCL patients and is correlated with advanced stage disease. Moreover, treatment with crizotinib, an anti-cancer drug inhibiting the c-Met/Hepatocyte growth factor receptor tyrosine kinase, blocks cell proliferation in CTCL cell lines.

CONCLUSIONS: These new data provide a promising rationale for using c-MET inhibition by the highly selective agents as a therapeutic modality of CTCL.

Scientific Session F. Biomarkers

F-07 BIOLOGICAL AND CLINICAL SIGNIFICANCE OF TRYPTOPHAN CATALYZING ENZYMES IN PATIENTS WITH CUTANE-OUS T-CELL LYMPHOMA

ORAL Maliniemi P, Väkevä L*, Lipsanen T, Jeskanen L, Dettmer K, Bessede A, Oefner PJ, Kadin ME, Ranki A

Department of Dermatology and Allergology, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland; Institute of Functional Genomics, University of Regensburg, Regensburg, Germany; ImmuSmol, Pessac, France; Department of Dermatology, Boston University School of Medicine and Roger Williams Medical Center, Providence, RI, USA

INTRODUCTION: Indoleamine 2,3-deoxygenase 1 (IDO) induces immune tolerance in the tumor microenvironment (TME) and is recognized as a potential new therapeutic target. We studied the expression and enzymatic activity of IDO in several different sub-types of a lymphoid malignancy, cutaneous T-cell lymphoma (CTCL), and evaluated the kynurenine (KYN) pathway in the local TME and in patient sera.

METHODS: Samples from the total of 91 patients with mycosis fungoides (MF, n=37), lymphomatoid papulosis (LyP, n=36), primary cutaneous anaplastic large cell lymphoma (pcALCL, n=4), subcutaneous panniculitis-like T-cell lymphoma (SPTCL n=4), and inflammatory lichen ruber planus (LRP, n=10), were analyzed by immunohistochemistry (IHC), immunofluorescence (IF), quantitative PCR, and/or liquid chromatography-tandem mass spectrometry (LC-MS/MS). MyLa and Mac1/2A cell lines were also studied.

RESULTS: Expression of both *IDO* and tryptophan-2,3-dioxygease (*TDO*) was up regulated in CTCL. In MF specimens and in MyLa2000 cell line, *IDO* expression exceeded that of *TDO*, while the opposite was true for LyP, ALCL, and ALCL cell lines. The spectrum of IDO-expressing cell types differed among the studied CTCL subtypes and reflected in the clinical behavior. In MF, SPTCL, and LyP, IDO was expressed by malignant cells and by CD33⁺ myeloid-derived suppressor cells, while in SPTCL CD163⁺ tumor-associated macrophages also expressed IDO. Significantly elevated serum KYN/Trp ratios were found in patients with advanced stages of MF. Epacadostat, an IDO inhibitor, induced a clear decrease in the KYN concentration in cell culture.

CONCLUSIONS: These results show the importance of IDO/KYN-induced immunosuppression in CTCL and suggests that blocking IDO activity might improve therapeutic responses in CTCL in combination with other therapies.

F-08 CELL ADHESION MOLECULE 1 IS A BIOMARKER FOR LEUKEMIC CELLS IN PROGRESSIVE OR REFRACTORY SÉZARY SYNDROME

ORAL Iwatsuki K*1, Yamaguchi M1, Hamada T1, Sugaya M2, Miura M3, Ohshima K3, Morishita K4

Depts. of Dermatol., ¹Okayama University Hospital, Okayama, and ²Tokyo University Hospital, Tokyo, ³Dept. of Pathology, School of Medicine, Kurume University, Fukuoka, and ⁴Dept. Medical Science, University of Miyazaki, Miyazaki, Japan

INTRODUCTION: Sézary syndrome (SS) is a rare leukemic variant of cutaneous T-cell lymphoma. We studied the expression of cell adhesion molecule 1 (CADM1) in the leukemic cells and skin infiltrates of SS patients, and we further examined the splicing variants and soluble form in the patients' sera.

METHODS: Peripheral blood mononuclear cells (PBMCs) from ten patients with SS, and eight lymphoma cell lines were assayed by flow cytometry. Skin biopsy specimens from patients with SS, mycosis fungoides (MF), and other types of lymphomas were examined for CADM1 expression by immunohistochemistry. Splicing variants of CADM1 were studied by RT-PCR and sequencing. Serum soluble CADM1 was assayed by ELISA.

RESULTS: Of 11 blood samples from ten SS patients, seven contained increased percentages of the CADM1+ cells in the CD3+CD4+ fraction (range: 6.2%–74.5%). No increase of CADM1+ cells (<4.95%) was observed in the sera from patients with indolent SS, MF, inflammatory skin diseases or CD3/CD28-stimulated normal lymphocytes. Two of three MF/SS-derived cell lines expressed CADM1 at 99.3% and 99.7%, respectively, and cell lines derived from adult T-cell leukemia/lymphoma (ATLL) and anaplastic large cell lymphoma (ALCL) expressed it to a lesser extent. CADM1+ cells were observed in the skin lesions of SS, MF, ATLL, and ALCL to varying degrees, but in smaller numbers than CCR4+ cells. Two major CADM1 splicing variants expressed by circulating Sézary cells contained combinations of the exons 7, 8, 9 and 11. Soluble CADM1 was not significantly elevated in SS sera.

CONCLUSIONS: CADM1 was shown to be a diagnostic cellular marker for progressive/refractory SS.

F-09 A REACTIVATION SIGNAL, BZLF-1, IS A BIOMARKER FOR SEVERE PHENOTYPES OF CUTANEOUS EBV-ASSOCIATED T/NK LYMPHOPROLIFERATIVE DISORDERS

ORAL Iwatsuki K*1, Hiorai Y1, Miyake T1, Yamamoto T1,2

Departments of Dermatology, ¹Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, ²Kawasaki Medical School, Kurashiki, Japan

INTRODUCTION: Cutaneous EBV-associated T/NK-LPDs include hydroa vacciniforme (HV), and hypersensitivity to mosquito bites (HMB). To study biomarkers related to the prognosis.

METHODS: We examined EBV reactivation markers in the tissue and blood samples from patients with HV and HMB by RT-PCR, and compared them with the systemic symptoms and survival rates.

RESULTS: An immediate-early reactivation marker, *BZLF1* mRNA was detected in 5 of 15 (33%) tissue samples from patients with systemic HV and/or HMB, but negative in classical HV. *BZLF1* mRNA was rarely detected in the blood samples. A down-stream

Scientific Session F. Biomarkers

reactivation signal, *BDRF1* mRNA was expressed in all 6 EBV+ epithelial neoplasms, but it was positive in only one of 15 (6.7%) samples from systemic HV and HMB in the tissue. EBV+ T/NK-cell line cells treated with PMA produced *BZLF1* and *BDRF1* mRNA, and encapsidated EBV DNA in the culture supernatants to a varying degree. In addition to the clinical phenotypes, univariate analysis in HV and HMB revealed 2 poor prognostic indicators: onset age of over 9 years, and *BZLF1* mRNA expression. Stimulation-induced EBV reactivation occurred both in vivo and in vitro, but it was almost abortive in vivo.

CONCLUSIONS: Late onset and EBV reactivation are both related to more severe phenotypes of the disease, and thus may predict a poor prognosis.

F-10 THE ROLE OF MATRIX METALLOPROTEINASE-2 PROMOTER GENOTYPE AND ITS IMMUNOHISTOCHEMICAL EX-PRESSION WITH SPECIFICITY PROTEIN-1 TRANSCRIPTION FACTOR IN THE EARLY DIAGNOSIS OF MYCOSIS FUNGOIDES POSTER EI-Sayed MH¹, Sallam MA¹, Osman WM², Ibrahim MA^{1*}

¹Department of Dermatology and Venereology, Faculty of Medicine, Ain shams university, Cairo, Egypt. ²Department of Pathology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

INTRODUCTION: Specificity protein-1 (Sp-1) is one of the transcriptional factors that promotes the oncogenetic effect of matrix metalloproteinase-2 (MMP-2) gene in many cancers however, scarce data are available on MMP-2 and Sp-1 transcription factor in early mycosis fungoides (MF). This study aimed to evaluate MMP-2 promoter gene polymorphism and the immunohistochemical expression of both MMP-2 and Sp-1 in early MF.

METHODS: This case-control study included 25 patients with early MF and 25 controls with chronic eczema in the period (2013-2014). MMP-2 promoter gene polymorphisms (-1575 G/A, -1306 C/T, -790 T/G) were studied by polymerase chain reaction with restriction fragment length polymorphism (PCR/RFLP) on formalin fixed paraffin blocks (FFPB). Immunohistochemical staining was also performed on FFPB using MMP-2 and Sp-1 polyclonal anti-rabbit antibodies.

RESULTS: Compared with controls, all MF patients showed no significant difference regarding genotype and allele distribution in all the studied polymorphism. As regards (-1306C/T), case-case analysis revealed that CC genotype was found in 76% of classical MF, whereas CT genotype was found in 75% of hypopigmented MF. MMP-2 immunohistochemical expression was found in 64% of the lymphocytic infiltrate and 76% of the stroma in MF patients whereas 16% of the lymphocytic infiltrate and 36% of the stroma in controls were positive. Sp-1 was expressed in 80% of the lymphocytic infiltrate of MF patients versus 44% in controls.

CONCLUSIONS: MMP-2 promoter gene polymorphism cannot be used as a diagnostic biomarker for early MF. Classical and hypopigmented MF showed different 1306 genotypes that may explain the difference in their clinical behavior. Both MMP-2 and Sp-1 can be used as diagnostic markers and may also throw the light on the possibility of targeting MMP-2 and Sp-1 in the treatment of early MF.

F-11 A MICRORNA BASED CLASSIFIER IN DIAGNOSIS AND PROGNOSIS OF CUTANEOUS T CELL LYMPHOMA

POSTER Wang B*, Li K, Zhao X, Xue F, Shi R, Shen X, Zheng J Department of Dermatology, Ruijin Hospital, Shanghai, China

INTRODUCTION: Cutaneous T cell lymphoma (CTCL) has a clinical and histological resemblance to the benign inflammatory dermatosis (BID), thus proven difficult to diagnose especially at the early stage of CTCL. Based on 228 patients, we aimed to identify a microRNA classifier to facilitate diagnosis and prognosis of CTCLs in Chinese Han population.

METHODS: Discovery Phase: A cross-platform miRNA microarray identified 9 miRNA that are differentially expressed between 50 CTCL and 20 BID patients. Training Phase: rtPCR validation on 58 CTCL and 25 BID patients provided a diagnosing classifier of 5 miRNAs. Test Phase: Accuracy of classifier was evaluated in an independent cohort of 50 CTCL and 25 BID patients.

RESULTS: Our 5 microRNA based classifier showed high diagnostic accuracy in CTCL (AUC=0.989 and 0.966 for training and test set, respectively). The classifier also provided high diagnostic value differentiating early MF with BIDs. We further examined the diagnostic value of each 9 miRNAs identified from discovery phase.

CONCLUSIONS: Our work provided the first miRNA-based classifier in Chinese Han population to facilitate CTCL diagnosis. These candidate miRNA also showed diagnostic value to CTCL progression. It may as well provide mechanistic insight to different CTCL pathogenesis between Asian and Caucasian populations.

* indicates presenting author

Scientific Session G. Genetics

G-01 VALIDATION AND FUNCTIONAL INTERROGATION OF JAK AND STAT VARIANTS IN PRIMARY CUTANEOUS T-CELL LYMPHOMA (CTCL)

ORAL Butler RM*1, Mosquera NC1, John S2, Whittaker SJ1, Mitchell TJ1

¹St John's Institute of Dermatology, Division of Genetics and Molecular Medicine, King's College London, London, England; ²Division of Immunology, Infection & Inflammatory Disease, King's College London, London, England

INTRODUCTION: Next generation sequencing (NGS) screens in CTCL tumours, including work from our own group, have identified the JAK and STAT genes as being commonly and recurrently mutated¹⁻²; these genes encode Janus Kinase (JAK) and Signal Transducer and Activator of Transcription (STAT) proteins, respectively. This study aims to validate and address the functional significance of the following JAK/STAT mutations: JAK1 p.R549Q, JAK2 p.H671Y, STAT3 p.N265S, p.Y640F, STAT5A p.P267A, p.L313P, p.A510V and STAT5B p.E150Q, p.E433K, p.E438K, p.N642H, p.Y665F¹⁻⁴.

METHODS: Non-synonymous JAK and STAT variants were validated in serial tissue samples from multiple tumour compartments (blood, lesional skin, lymph node) and tumour-derived cDNA using Sanger sequencing. Mutant STAT3, STAT5A and STAT5B constructs were generated by site-directed mutagenesis and transiently expressed in HEK293T cells. STAT activity was assayed by immunoblot and STAT luciferase reporter assays. Statistical significance was assessed using two-tailed Student's t-tests with Bonferroni correction.

RESULTS: The NGS screen within our group identified non-synonymous, tumour specific JAK and STAT variants in 14% (14/101) of Sézary tumours². Variants persisted at the genomic and transcriptional level within serial tumour samples from multiple affected tissue sites, whilst variants were absent in patients who achieved complete remission after reduced-intensity stem cell transplant (RISCT). Increased STAT phosphorylation in unstimulated cells was detected with 5/10 STAT variants by immunoblot. Significantly increased functional activity was confirmed using luciferase reporter assays. These findings demonstrated for the first time that the STAT5B p.E433K³ and p.E438K⁴ variants increased STAT activity ($p \le .5x10^4$) and confirmed previous work for the STAT3 p.Y640F⁵, STAT5B p.N642H⁶⁻⁷ and p.Y665F⁸ variants ($p \le 1.5x10^6$).

CONCLUSIONS: This study demonstrated that non-synonymous *JAK/STAT* variants persisted in Sézary tumours over time in multiple affected tissues. Constitutive STAT activation was demonstrated for 5/10 variant STAT constructs; this strengthens the hypothesis that JAK-STAT signaling, which mediates T-cell proliferation and survival, is dysregulated in CTCL. Importantly, this study identified two STAT5B DNA-binding domain mutants, E433K³ and E438K⁴, as gain-of-function mutants. Future work will screen gain-of-function mutants against libraries of small molecular inhibitors with the aim of identifying novel therapeutic targets for aberrant JAK-STAT signalling in CTCL.

References: 1. Kiel, M. J. et al. (2015). Nat. Commun. 6, 8470. 2. Woollard, W. J. et al. (2016). Blood. 10.1182/blood-2016-02-699843. [Epub ahead of print]. 3. Ungewickell, A. et al. (2015). Nat. Genet. 47, 1056–60.4. Da Silva Almeida, A. C. et al. (2015). Nat. Genet. 47, 1465–70.5. Koskela, H. L. M. et al. (2012). N. Engl. J. Med. 366, 1905–13.6. Yamada, K. et al. (2000). Int. J. Hematol. 71, 46–54.7. Bandapalli, O. R. et al. (2014). Haematologica. 99, e188–92.8. Rajala, H. L. M. et al. (2013). Blood. 121, 4541–50

G-02 DIRECT GENE EXPRESSION MEASUREMENT IN SKIN HELPS PREDICT LONG-TERM CLINICAL OUTCOME IN PA-TIENTS WITH CUTANEOUS T-CELL LYMPHOMAS

ORAL De Masson A*, O'Malley JT, Elco CP, Garcia S, DiVito SJ, Lowry EL, Teague JE, LeBoeuf NR, Robins H, Clark RA, Kupper TS Department of Dermatology, Center for Cutaneous Oncology, Dana Farber / Brigham and Women's Cancer Center, Harvard Medical School, Boston, USA and Adaptive Biotechnologies, Seattle, USA.

INTRODUCTION: Cutaneous T-cell lymphomas (CTCL) are rare diseases that share a good prognosis in the early stages. However, some patients progress to advanced-stage, aggressive disease. Early identification of the molecular factors that govern CTCL progression could enable a personalized treatment strategy. We and others previously identified genes recurrently differentially expressed in CTCL progressors as compared to patients with stable disease. This study aims at studying what molecular factors can add to the existing knowledge in terms of prognostic factors in CTCL.

METHODS: Patients with primary CTCL were prospectively included in the DFCI 02016 study at Dana Farber Cancer Institute from 2002 to 2016 and gave informed consent. Disease stage and progression were assessed using the international ISCL/EORTC criteria for CTCL. Disease stage, age of the patient, the existence of folliculotropism and large-cell transformation, as well as LDH levels were recorded at the time of the biopsy. DNA and RNA were extracted from archival, formalin-fixed, paraffin-embedded lesional skin biopsies from 178 study patients. Additionally, a biopsy before and after progression were studied in 10 patients. Gene expression levels of 78 genes previously identified as potential biomarkers of disease progression were measured using Nanostring. The reliability and reproducibility of the Nanostring technique were first confirmed by comparing Nanostring and Affymetrix gene expression levels in 48 frozen RNA samples from CTCL patients. Additionally, high throughput sequencing data of the TCR beta gene were obtained from each sample to measure the relative amount of T cells, the frequency of the tumor clone, frequency of reactive clones and the entropy. A univariate Cox analysis was carried out to identify molecular variables associated with progression-free survival. A stepwise selection process was used to select variables to be studied in multivariate analysis in association with age, disease stage, histologic factors and LDH levels as covariates.

RESULTS: This study confirms the usefulness of molecular factors to refine the prognosis in cutaneous T-cell lymphomas and identifies pathways which are recurrently involved in disease progression and could represent potential therapeutic targets.

CONCLUSIONS: This monocentric, relatively large-scale study confirms the feasibility of the use of archival, FFPE samples from

CTCL patients to study molecular prognostic factors with long-term follow-up times. It identifies genes recurrently differentially expressed in progressors and precises the role of TCR sequencing data as prognostic factors in CTCL. This model will be confirmed on an independent cohort.

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Scientific Session G. Genetics

G-03 DEVELOPMENT OF AN IN VITRO CTCL PLATFORM FOR SCREENING TARGETED MOLECULAR AGENTS

ORAL Weed J*, Lewis J, Carlson K, Foss F, Girardi M Yale School of Medicine, New Haven, United States

INTRODUCTION: Recent genomic and transcriptomic studies^{1,2} have captured the genetic and transcriptional landscape of leukemic cutaneous T cell lymphoma at a higher-resolution than previously possible, with recurrently identified mutations and RNA expression level variations suggesting targetable pathways driving disease activity. Informed by these advances, we selected a panel of approved and investigational targeted therapies to correlate drug responses of isolated CTCL cells with patient gene copy/ mutational status utilizing an 11-probe fluorescence in situ hybridization (FISH) probe panel, in association with pathway-specific expression levels.

METHODS: Towards a personalized medicine screening protocol, we employed an in vitro screening assay for drug susceptibility involving magnetic bead sorting of peripheral blood to enrich for malignant populations, typically CD3+CD4+CD26- and/or CD7-T cells, followed by 12 to 72 hour cell culture with exposure to select (including off-label) agents over a range of concentrations. Screened targeted pathways included established CTCL effector targets, e.g. HDAC inhibition, as well as suspected/potential CTCL effector targets, e.g. proteasome inhibition, BH3 mimetic inhibition, and bromodomain inhibition.

RESULTS: Cytotoxic/cytostatic effects were assessed as apoptosis induction via caspase-3 and -7 activation and as the change in cell viability via media ATP quantitation. Sensitivity to cytotoxic effects of tested agents was highly variable among CTCL patient samples and established CTCL lines, with EC50 values ranging from under 3 nM to over 20 µM. In certain circumstances, our preliminary data suggest a potential relationship between measured IC50 values and gene expression levels.

CONCLUSIONS: We present the feasibility of a patient-based in vitro screening platform to assess the susceptibility of leukemic CTCL cells to targeted therapeutics in correlation with specific biomarkers.

G-04 LESSONS LEARNED FROM A NOVEL MOUSE MODEL OF CTCL

ORAL Fanok MH^{1,\$}, Sun A^{1,\$}, Fogli LK^{1,\$}, Narendran V², Kannan K^{1,3}, Dolgalev I^{1,3}, Heguy A^{1,3}, Sundrud MS⁴, Liu C¹, Kutok J^{5‡}, Latkowski J⁶, Aifantis I^{1,7}, Ødum N⁸, Hymes KB^{2,7}, Goel S^{2,§}, Koralov SB^{*1,7}

¹Department of Pathology, NYU School of Medicine, New York, NY 10016. ²Department of Medicine, Division of Hematology-Oncology, NYU School of Medicine; New York, NY 10016. ³Office of Collaborative Science, NYU School of Medicine; New York, NY 10016. ⁴Department of Cancer Biology, The Scripps Research Institute; Jupiter, FL 33458. ⁵Department of Pathology, Brigham and Women's Hospital; Boston, MA 02115. ⁶Department of Dermatology, NYU School of Medicine; New York, NY 10016. ⁷Laura and Isaac Perlmutter Cancer Institute, NYU School of Medicine; New York, NY 10016. ⁸Department of International Health, Immunology and Microbiology, University of Copenhagen; Copenhagen, Denmark. [‡] Present address: Biology and Translation Science, Infinity Pharmaceuticals, Inc; Cambridge, MA 02139. § Present address: Department of Medicine, Division of Hematology, Albert Einstein College of Medicine; Bronx, NY 10467. ^{\$} These authors contributed equally.

INTRODUCTION: Currently, the molecular etiology of Mycosis Fungoides and Sézary Syndrome (the most frequent forms of Cutaneous T Cell Lymphoma) remains enigmatic. Our goal was to take advantage of next generation sequencing of primary patient biospecimens to dysregulated pathways critical to the pathogenesis of this malignancy and to use conditional gene targeting to demonstrate causality.

METHODS: We took advantage of next generation sequencing to explore the genetic changes in the malignant cells isolated from Sézary patients by comparing the genome of these cells to non-transformed hematopoeitic cells isolated from the same patients. We then took advantage of conditional gene targeting to generate a hundred percent penetrant mouse model of CTCL by targeting the JAK/STAT signaling pathway that we identified to be frequently hyperactivated in this malignant disease. We then carefully characterized the malignant disease in this novel animal model and demonstrated that the disease faithfully recapitulates many of the pathognomonic features of human disease.

RESULTS: Our whole exome sequencing (WES) of a cohort of SS patients revealed a heterogeneous spread of genetic alterations that converged on several oncogenic pathways, including *PI3K* signaling and *STAT* (Signal Transducer and Activator of Transcription) 3 pathway. Critically, analysis of high throughput RNA sequencing data from malignant T cells highlighted a *STAT3* and *PI3K* gene expression signature among the malignant lymphocytes. Using conditional gene targeting to express a hyperactive allele of STAT3 selectively in T lymphocytes, we generated a novel animal model of CTCL that recapitulates many of the key features of human disease.

CONCLUSIONS: Generation of this animal model of CTCL demonstrates the causative role of dysregulated STAT3 signaling in CTCL pathogenesis and establishes a tractable pre-clinical model for evaluation of novel therapeutic strategies for CTCL. Furthermore, we have now taken advantage of STAT3C animals rederived into germ-free isolators to explore the role of microbiota in CTCL pathogenesis and this will also be discussed.

Scientific Session G. Genetics

G-05 HIGH-THROUGHPUT T CELL RECEPTOR SEQUENCING TRANSFORMS CARE OF CUTANEOUS T CELL LYMPHOMA PATIENTS

ORAL O'Malley JT^{*1}, Kirsch I², Lowry E¹, Teague JE¹, Vieyra-Garcia P¹, Williamson DW², Elco C³, Teague JE¹, Gehad A¹, Robins H², Rook AH⁴, Kupper TS¹, Clark RA¹

¹Dept. Dermatology, Brigham and Women's Hospital and DF/BWH Cancer Center, Harvard Medical School, Boston, MA, USA. ²Adaptive Biotechnologies, Seattle, WA, USA. ³Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA. ⁴Department of Dermatology and the Center for Clinical Biostatistics and Epidemiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

INTRODUCTION: One major goal of our Center is to develop and implement high-throughput T cell receptor (TCR) sequencing (HTS) as a powerful tool to improve the diagnosis, follow up and prognosis of patients with CTCL. Our goals are to provide more rapid and definitive diagnoses, to determine which CTCL therapies actually kill malignant T cells vs. only suppressing visible inflammation, and to develop HTS as a means to discriminate early stage patients who are at high risk for eventual disease progression. METHODS: DNA derived from of blood and skin samples from CTCL patients, patients with other inflammatory diseases and

healthy controls were analyzed by high throughput TCR sequencing using ImmunoSEQ (Adaptive Biotechnologies, Seattle, WA). RESULTS: With respect to establishing a diagnosis of CTCL, we found that HTS was more sensitive and specific than TCRy PCR, detected T cell clones in 46/46 CTCL patients, and successfully discriminated CTCL from psoriasis, eczematous dermatitis and healthy skin. We compared low dose radiation (LDR), psoralen plus UVA (PUVA) and topical resiquimod and found that both LDR and topical resiquimod effectively depleted malignant T cells from skin but that in many patients treated with PUVA, clinical responses were not correlated with decreased numbers of malignant T cells and were associated with changes in the benign T cell population. Lastly, we have assembled a cohort of progressing vs. non-progressing early stage patients and we are in the process of developing potential metrics that will identify patients who will develop progressive disease.

CONCLUSIONS: HTS is a powerful clinical and research tool that can enhance diagnosis, identify which treatment regimens actually kill malignant T cells and potentially identify patients at high risk for disease progression.

G-06 TCR SEQUENCING FACILITATES DIAGNOSIS AND IDENTIFIES MATURE T CELLS AS THE CELL OF ORIGIN IN CUTA-NEOUS T-CELL LYMPHOMA

ORAL Kirsch IR*¹, Watanabe R², O'Malley JT², Williamson DW¹, Scott LL², Elco CP³, Teague JE², Gehad A², Lowry EL², LeBoeuf NR⁴, Krueger JG⁵, Robins HS¹, Kupper TS⁶, Clark RA⁶

¹Adaptive Biotechnologies, Seattle, WA 98102, USA. ²Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA. ³Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA. ⁴Dana-Farber/Brigham and Women's Cancer Center, Boston, MA 02115, USA. ⁵Department of Dermatology, Rockefeller University, New York, NY 10065, USA.

INTRODUCTION: Early diagnosis of cutaneous T cell lymphoma (CTCL) is difficult and takes on average 6 years after presentation, in part because the clinical appearance and histopathology of CTCL can resemble that of benign inflammatory skin diseases. A more reliable method of discriminating between CTCL and benign inflammatory skin disease would both facilitate timely diagnosis of the disease and help to discriminate CTCL recurrences from unrelated benign inflammatory reactions in the skin.

METHODS: We analyzed DNA from punch biopsies of 46 CTCL skin lesions, lesional skin from 23 patients with psoriasis, 11 patients with eczematous dermatitis, 12 patients with contact dermatitis, 12 patients with PLEVA, and the skin of 6 healthy donors by high throughput sequencing (HTS) for both the TCR Vg and TCR Vb. Clonality values were calculated from entropy of the TCR Vb CDR3 frequency distribution and then normalized by log (number of unique TCRVb CDR3). Clonality values range from 0 (polyclonal distribution) to 1 (monoclonal distribution). In certain cases, blood samples from study patients were analyzed for the presence or absence of index clonal sequences identified within the diagnostic skin lesions.

RESULTS: High-throughput TCR CDR3 region sequencing identifies expanded T cell clones and discriminates CTCL from benign inflammatory skin disorders. HTS is informative in patients with negative clonality assessments by conventional TCRg PCR. HTS discriminates CTCL recurrences from benign inflammation, provides accurate assessment of responses to therapy, and facilitates early diagnosis of disease recurrence in both the skin and blood of patients with CTCL. In patients with new discrete skin lesions and no clinical involvement of peripheral blood, HTS demonstrates hematogenous of malignant T cells. HTS TCRg gene studies demonstrate that CTCL is derived from mature T cells. MF and L-CTCL malignant T cells localize to distinct anatomic compartments in the skin.

CONCLUSIONS: A multiplex PCR and high throughput sequencing assay accurately diagnosed CTCL in all stages, discriminated CTCL from benign inflammatory skin diseases, and provided insights into the cell of origin and location of malignant CTCL cells in skin.

Abstracts Scientific Session G. Genetics

G-07 INTEGRATIVE ANALYSIS OF GENOMIC DATA TO IDENTIFY COMMON GENOMIC ALTERATIONS IN CUTANEOUS T-CELL LYMPHOMA

ORAL Chang LW*, Patrone CC, Ferrando A, Palomero, T[#], Geskin LJ[#] *Co-senior authors

Department of Dermatology, Columbia University, New York; Institute for Cancer Genetics, Columbia University.

INTRODUCTION: Recent studies have used high throughput sequencing to characterize the genomic landscape of cutaneous T-cell lymphoma (CTCL). However, due to disease rarity and genomic heterogeneity of CTCL, discovering genes or pathways that play a central role in CTCL pathogenesis remains challenging.

METHODS: We co-analyzed six recently published genomic datasets of cutaneous T cell lymphoma. A combined cohort of CTCL samples, including 89 Sézary syndrome and 19 mycosis fungoides, were assembled from previous studies. A total of 9537 genomic mutations including single nucleotide substitutions, insertions and deletions was compiled, and Poisson statistics were used to identify recurrently mutated genes and pathways in CTCL. In parallel, we combined eight published high-resolution datasets of gene copy number profiling in CTCL, generating a combined cohort of 112 Sézary syndrome and 87 mycosis fungoides patients. Genomic regions of copy number change reported in individual studies were co-analyzed in order to identify frequently amplified or deleted regions in CTCL.

RESULTS: We found recurrent mutations in genes previously implied in CTCL pathogenesis, including those involved in gene regulation, NFkB pathway, signal transduction and epigenetic regulation. The most frequently mutated genes were *TP53* (18%), *PLCG1* (9%), *ARID1A* (9%), *CARD11* (8%) and *TNFRSF1B* (7%). We also identified frequently mutated genes that were not highlighted in previous studies. Our copy number analysis validated frequent deletion in 17p and 10q and gain in 17q and 8q. We also identified mycosis fungoides specific gain in 1p, 1q, 7p, and 7q and loss in 9p, 13q and 16q. In contrast, Sézary syndrome specific alterations include narrow chromosomal gain in 2p, 3q, 10p and loss in 11q, 12p and 19p.

CONCLUSIONS: This study validated previously reported genomic alterations in CTCL and identified additional frequently mutated genes that may be important in CTCL pathogenesis. Additional patient cohorts and functional studies may be required to further characterize the role of these genes in CTCL.

G-08 GENOMIC LANDSCAPE OF MYCOSIS FUNGOIDES

ORAL Yoo J*1, Beggs A², Noyvert B³, Murray D⁴, Cazier JB³, Stockton J², Shah F¹, Stevens A⁵, Chaganti S⁶, Moss P⁴, Scarisbrick JJ¹ ¹Department Dermatology, ² Wellcome Trust, University of Birmingham, ³ Centre for Computational Biology, University of Birmingham, ⁴ Institute of Immunology & Immunotherapy, University of Birmingham, ⁵Oncology, ⁶Haematology, University Hospital Birmingham, Birmingham, UK

INTRODUCTION: Recent next generation sequencing (NGS) revealed marked genomic heterogeneity in mycosis fungoides (MF) and identified several common gene abnormalities (TCR, JAK-STAT and NF**k**B signalling) as well as abnormal epigenetic regulation but none are considered causative of MF. To identify potential drivers of MF, we performed whole-exome sequencing (WES) on MF skin lesions.

METHODS: We performed WES on DNA from 9 MF skin lesions (2xpatch, 4xplaque, 3xtumours) from 6 patients (stage IB:n=2, IIB:n=4) and patient matched normal DNA (Illumina Nextera rapid capture exome kit). Reads were aligned using the Burrows-Wheeler Aligner. Somatic variants were detected using MuTect and annotated with SnpEff.

RESULTS: Recurrent mutations found in 3 or more samples from different patients included the following genes: HLA-DRB5, LAMA1, OR2L8, PLA2R1, TPP2, PPL, ARHGAP23. When we only included the 3 MF tumours for analysis, TPP2, PLA2R1, OR2L8 and LAMA1 were identified in 2 of 3 patients without this mutation present in patch/plaque lesions from the same patient. Increasing cytosine to thymine substitution was observed from patch to tumour with signature profile similar to skin cancer related ultraviolet light exposure in one patient who had previous phototherapy.

CONCLUSIONS: It has been proposed that MF arises from a state of chronic antigenic stimulation in genetically susceptible individuals. Human leucocyte antigen (HLA)-DRB5 (HLA-DRB1*11), which plays a central role in the immune system by presenting antigens from extracellular proteins to T-lymphocytes, has been shown to have significantly increased frequency in MF. Our study showed HLA-DR5 mutation in 5 MF samples from 2 patients which may support an association between HLA-DR5 and MF.

We identified TPP2, PLA2R1, OR2L8 and LAMA1 abnormalities in tumours without these mutations in patch/plaque lesions from the same patient. If we can identify the driver genetic mutations associated with MF progression from patch to plaque to tumour then these could possibly be developed as targeted treatment for MF. Genomic studies on patches, plaques and tumours from individual patients in a larger cohort from our centre are ongoing and may help support these findings.

Scientific Session G. Genetics

G-09 IDENTIFICATION AND VALIDATION OF MITOGEN-ACTIVATED PROTEIN KINASE (MAPK) PATHWAY GENE MUTA-TIONS IN SÉZARY SYNDROME

POSTER Flanagan C^{*}, Whittaker SJ, Mitchell TJ

St Johns Institute of Dermatology, Division of Genetics and Molecular Medicine, Tower Wing, Kings College London, Great Maze Pond, London, SE1 9RT, United Kingdom.

INTRODUCTION: The molecular pathways involved in the pathogenesis of CTCL remain poorly defined. We have used a next-generation sequencing (NGS) approach, comprising a discovery and prevalence screen to identify recurrently mutated genes and dysregulated pathways in Sézary Syndrome (SS) tumour cells.

METHODS: Patient samples were obtained from the nationally approved CTCL research tissue bank (National Research Ethics Committee: 07/H10712/111+5). Paired-end libraries were sequenced on an Illumina Hi-Seq2000. The discovery screen used whole exome sequencing of DNA from CD4+ tumour cells and matched fibroblast DNA from 10 untreated SS patients followed by systematic bioinformatic filtering to identify somatic, non-synonymous variants. The prevalence screen used targeted capture sequencing of 549 genes in PBMC DNA from 101 SS patients and 32 healthy controls. Gene set enrichment analysis using the MSigDB repository was used to identify significant pathway perturbations. Variants were validated by PCR/Sanger sequencing. Pathogenicity prediction tools were used to prioritise variants.

RESULTS: A total of 824 somatic non-synonymous gene variants were identified including indels, stop gain/loss, splice variants and recurrent gene variants indicative of considerable molecular heterogeneity. Genomic aberrations identified were enriched for genes implicated in: genomic stability (*POT1* and *ATM*); TCR/NFkB signalling (PDGFR, ERK, JAK STAT, MAPK); epigenetic regulation (*DN-MT3A*, *ASLX3*, *TET1-3*) and homologous recombination (*RAD51C*, *BRCA2*, *POLD1*). The mitogen-activated protein kinase (MAPK) pathway was one of the most frequently perturbed pathways with 68 variants in 13 genes, affecting 56/101 SS tumour samples. Seven MAPK pathway genes (16 variants) were selected for further investigation. The presence of 14/16 variants were confirmed and demonstrated in serial samples, from multiple tumour compartments (blood, skin, lymph node) in DNA and RNA. Pathogenicity prediction algorithms, variant-protein mapping and conservation analysis suggest that all variants are likely to be pathogenic.

CONCLUSIONS: Five genes in the MAPK pathway, PDGFRA, PPP5C, RASGRP4, NFATC2 and TGFBR1 were identified as potential drivers of SS and are the focus of on-going functional studies. Targeting the MAPK pathway may represent an attractive potential therapeutic strategy for CTCL.

Reference: Woollard et al: Blood. 2016 Apr 27. pii: blood-2016-02-699843. Epub ahead of print

G-10 A LARGE GROUP OF K111 PERICENTROMERIC HUMAN ENDOGENOUS RETROVIRUSES ARE LIKELY MISSING ("NULL K111") IN PATIENTS WITH SEVERE FORMS OF CUTANEOUS T CELL LYMPHOMA

POSTER Kaplan MH², Galindo R², Tejasvi T^{*1,3}, Kaminiski M², Estes J², Gitlin SD², Mohammad S⁴, Markovitz D², Elder JT^{1,3} ¹Department of Dermatology,²Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan; ³Ann Arbor Veteran Health Services, Ann Arbor, Michigan; ⁴Institute of Human Virology University of Maryland

The majority of cutaneous T cell lymphoma (CTCL) patients follow an indolent course and can be effectively managed with skin-directed therapies. Occasionally, some patients progress to poorer prognostic stages with development of tumors, large cell transformation, and other complications. There are no biomarkers to predict outcomes of CTCL. Recently a new group of HERV K HML-2 human endogenous retroviruses, K111, were discovered to be present in the pericentromeric region of the human genome with as many as 1,000 proviruses predominantly located on chromosomes 21 and 22. Surprisingly, some Caucasians lack this group of viruses ("null K111"), especially those with severe forms of CTCL. Peripheral blood DNA was screened for the K111 virus, by guantitative polymerase chain reaction (gPCR), using primers in the CER element and in the gag gene of K111. Patients with the null K111 genotype were missing a 1650bp fragment, indicative of having no K111 viruses in their pericentromeric area. We screened for this genotype in Caucasians with severe CTCL and other disorders. Thirteen of 39 patients with severe CTCL [i.e. advanced disease requiring chemotherapy (37), Sezary Syndrome (SS) (11), large cell transformation (11)] were found to manifest the null K111 genotype [0/5 African Americans and 13/34 (41%) of Caucasians]. Five of 11(45%) Caucasian patients with SS had the null K111 genotype. In contrast, in Caucasians with other disorders only 45/333 (13.5%) had this genotype, including 13/95 with psoriasis, 6/48 with breast cancer, 7/46 with other lymphomas, 6/ 48 HIV patients and 13/ 96 normal controls. This difference was statistically significant (p= 0.016 by Chi square test). qPCR demonstrated that patients with severe CTCL also had lower copy numbers of K111 proviruses in their genome overall. Conclusion: The null K111 genotype is associated with more severe forms of cutaneous T cell lymphoma and may prove to be a useful marker for poor prognosis for this disease.

* indicates presenting author

Abstracts

Scientific Session H. Cutaneous B-cell Lymphomas

H-01 IMMUNOGLOBULIN CONSTANT REGION MUTATIONS IN PRIMARY CUTANEOUS DIFFUSE LARGE B-CELL LYMPHO-MA, LEG TYPE

ORAL Koning MT*1, Übelhart R², van der Zeeuw SA³, Koens L⁴, Schmidt CA⁵, Przybylski G⁵, Kielbasa SM³, Jumaa H², Vermeer MH⁶, Willemze R⁶, Tensen CP⁶, Veelken H¹

¹Department of Hematology, Leiden University Medical Center, Leiden, The Netherlands; ²Department of Immunology, University Medical Center Ulm, Ulm, Germany; ³Sequence Analysis Support Core, Leiden University Medical Center, Leiden, The Netherlands; ⁴Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands; ⁵Department of Molecular Hematology, Greifswald University, Greifswald, Germany; ⁶Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands

INTRODUCTION: Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type (DLBCL, LT) is a rare and aggressive neoplasm with a primary cutaneous presentation that shares genetic and phenotypic characteristics with DLBCL of activated B-cell subtype (ABC-DLBCL). The role of the B-cell receptor (BCR) in DLBCL-LT is largely unknown, but receptor stereotypes have been observed. Previous studies on small cohorts suggested that DLBCL-LT expresses IgM with overrepresentation of IGHV3 alleles and rates of somatic mutations. We aimed to elucidate the role of the BCR in DLBCL-LT.

METHODS: 8 cases of DLBCL-LT were subjected to RNAseq. Additional RNAseq data from healthy volunteers (Geuvadis) and 10 DLBCL non-LT were obtained from NCBI publicly available datasets. VDJ/VJ rearrangements and IgM constant regions were Sanger sequenced for all cases and two granulocyte controls. Lymphoma-derived, clonal BCR were tested for autonomous signalling activity in the murine TKO pre-B-cell system (Dühren-von Minden, Nature 2012).

RESULTS RNAseq analysis demonstrated an IgM isotype in all cases (8/8) and VJ-kappa in 7/8 cases. IGHV3 usage was observed in 7/8 cases (among which 4x IGHV3-7). DLBCL-LT BCR were strongly mutated (range: VDJ 3.1-22.2%; VJ 0.6-13.5%). No intraclonal sequence variation was observed. Non-synonymous single nucleotide variants (SNV) were observed in the IgM constant regions of 4/8 cases and IGKC of 1/8, but not in granulocyte DNA or in the other 16 RNAseq libraries. In contrast to ABC-DLBCL (Koning, AACR 2016), BCR of DLBCL-LT did not induce antigen-independent calcium flux in TKO cells upon induction of functionality of the BCR signalling cascade by tamoxifen.

CONCLUSIONS: Our data extend previously reported characteristics of the BCR expressed by DLBCL-LT. In contrast to CLL, BCR stereotypy was not associated with autonomous BCR signalling activity. Despite their phenotypic similarity, the lack of autonomous BCR signalling in DLBCL-LT points to a different pathogenetic role of the BCR compared to ABC-DLBCL. We aim to experimentally assess the functional consequences of the previously unreported, somatically acquired and tumour-specific mutations in the BCR constant region of DLBCL-LT on BCR signalling and antigen recognition.

H-02 THE B-CELL RECEPTOR OF PRIMARY CUTANEOUS FOLLICLE CENTER LYMPHOMA: IMPLICATIONS FOR PATHOGEN-ESIS

ORAL Koning MT*1, van der Zeeuw SA², Zoutman W³, Vermeer MH³, Willemze R³, Veelken H¹, Tensen CP³

¹Department of Hematology, Leiden University Medical Center, Leiden, The Netherlands. ²Sequence Analysis Support Core, Leiden University Medical Center, Leiden, The Netherlands. ³Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands

INTRODUCTION: Primary Cutaneous Follicle Center Lymphoma (PCFCL), a very indolent lymphoma, shares germinal centre (GC) morphology with follicular lymphoma (FL) but lacks the characteristic t(14;18). Unlike FL, immunohistochemistry fails to detect BCL2, CD10, and immunoglobulin in PCFCL. We investigated the B-cell receptor (BCR) to gain insight into the immunobiology of PCFCL. METHODS: Whole Genome Sequencing (WGS) and RNAseq were performed on 5 PCFCL biopsies. Full-length BCR transcripts were amplified by unbiased ARTISAN PCR (Koning et al, BJH 2016) and sequenced to >2000 sequences per transcript on the Pac-Bio platform.

RESULTS WGS identified a t(14;22), juxtaposing IGH and IGLL5, in one case. No case carried a t(14:18). ARTISAN PCR and RNAseq-based de novo BCR assembly independently demonstrated expression of functional VDJ and VJ genes with heavily mutated V regions (VDJ: 7,1-16,0%; VJ: 4,6-11,1%) in all cases. Lack of intraclonal sequence variations indicated absence of ongoing somatic hypermutation (SHM). The t(14;22)+ PCFCL expressed an inconspicuous IgM. BCR of all remaining four PCFCL carried SHM-acquired sequence motifs for N-linked glycosylation in antigen-binding regions as previously described for FL. Three cases had undergone class switch recombination to IgG. The remaining case expressed IgM with extensive mutations.

CONCLUSIONS: GC morphology, class switch recombination, and extensive SHM indicate a shared origin of GC B cells for PCFCL and FL. BCR sequences and previously identified copy number alterations prove that PCFCL represents a neoplastic clonal expansion. However, lack of ongoing SHM indicates that the immune follicles of PCFCL are not fully functional germinal centres. Since ongoing SHM is thought to contribute to lymphomagenesis by targeting non-BCR loci, absence of both ongoing SHM and the t(14;18) may explain the benign clinical course of PCFCL compared to FL. Further comparisons to define the extent of malignant transformation between PCFCL, FL, and other B-lymphomas are warranted. Continuous BCR stimulation through glycosylation-mediated binding of lectins on resident cells of the follicular microenvironment may explain the clonal expansion of PCFCL and could play a decisive role in maintaining the follicular microarchitecture in both FL and PCFCL.

Scientific Session H. Cutaneous B-cell Lymphomas

H-03 PD1 AND PD-L1 EXPRESSION IN PRIMARY CUTANEOUS DIFFUSE LARGE B CELL LYMPHOMA

ORAL Mitteldorf C*1, Berisha A², Tronnier M¹, Pfaltz M³, Broekaert S⁴, Kerl K⁵, Mertz K⁶, Kempf W²

¹Department of Dermatology, HELIOS-Klinikum Hildesheim, Germany; ²Kempf und Pfaltz, Histologische Diagnostik, Zürich, Switzerland; ³Department of Psychiatry and Psychotherapy, University Hospital Zürich, Switzerland; ⁴Department of Dermatology, University Hospital Göttingen, Germany, ⁵Department of Dermatology, University Hospital Zürich, Switzerland, ⁶Institute of Pathology, Liestal, Switzerland

INTRODUCTION: In nodal DLBL PD-L1 expression has been found in 24-82% of the tumors, depending on the examined tissue (frozen-tissue versus paraffin-embedded), the antibody and the subtype of DLBL (GCB versus ABC). PD-L1 expression in primary cutaneous DLBCL has not been investigated so far.

METHODS: We investigated 18 paraffin-embedded tissue samples of diffuse large B-cell lymphoma (DLBCL) (14 leg-type (LT), 4 other-type (OT)) for their PD-L1 expression by immunohistochemistry.

RESULTS: We observed a predominantly membranous expression of PD-L1 within the tumor cells in all of our investigated cases (all DLBL: mean 20,8%; LT: mean 19,7%, OT mean: 24,6%). Among DLBL LT tumors, 10 cases were subclassified as ABC-type and 2 as GCB-type, with a significantly lower PD-L1 score in GCB-type. In DLBL OT only 1 ABC-type and 3 GCB-types were found. The surrounding infiltrate was mild to moderate, consisting of T-cells, histiocytes and myeloid cells. The tumor cells were PD1 negative. The PD1 expression in tumor infiltrating lymphocytes (TIL) was higher in OT than in LT. Moreover we investigated CD33 expression, as an important marker for myeloid derived suppressor cells (MDCS). We demonstrated that the CD33 expression was predominantly intermediate with a diffuse distribution. In mean, 63,2% of the CD33 positive cells demonstrated a PD-L1 co-expression.

CONCLUSIONS: Our data imply that a therapy with an anti-PD-1 or anti-PD-L1 antibody might be promising therapeutic approaches. Moreover the high PD-L1 expression in the tumor cells might be one reason for the poor prognosis. We hypothesize that the PD-L1+ tumors cells and the PD-L1+ MDSC can induce apoptosis in TILs. This may explain the lower level of PD1+ TILs in DLBL in contrast to indolent primary cutaneous B-cell lymphoma, which has been recently published by our group.

H-04 PRIMARY CUTANEOUS DIFFUSE LARGE B-CELL LYMPHOMA, LEG-TYPE: HIGH FREQUENCY, DIAGNOSTIC AND PROGNOSTIC VALUE OF MYD88 L265P MUTATION

ORAL Pham-Ledard A^{*1,2}, Menguy S^{•(1,3)}, Barbe C⁴, Grange F^{5,6}, Petrella T^{5,7}, Martinez F⁸, Cappellen D^{1,8}, Vergier B^{1,3,5}, Beylot-Barry $M^{1,2,5}$, Merlio JP^{1,5,8}, and the French Study Group on Cutaneous Lymphomas

contributed equally to the study

¹INSERM U1053,Bordeaux research in Translational Oncology, Team 3 oncogenesis of cutaneous lymphomas, Univ. Bordeaux, France; ²Dermatology Department, CHU Bordeaux, Bordeaux, France; ³Pathology Department, CHU Bordeaux, Pessac, France; ⁴Department of clinical research, CHU Reims, Reims, France; ⁵French Study Group on Cutaneous Lymphomas, France; ⁶Dermatology Department, CHU Reims, Reims, France; ⁷Pathology Department, University of Montréal, Canada; ⁸Tumor Bank and Tumor Biology Laboratory, CHU Bordeaux, Pessac, France

INTRODUCTION: *MYD88*^{L265P} activating mutation is a frequent feature of primary cutaneous diffuse large B-cell lymphoma, leg-type (PCLBCL-LT), reported in up to 69% of cases, not confirmed by others. To investigate diagnostic and prognostic value of *MYD88*^{L265P} mutation among primary cutaneous B-cell lymphomas, we conducted two retrospective analysis.

METHODS: To evaluate diagnostic value of MYD88^{L265P} mutation among primary cutaneous large B-cell lymphomas, we retrospectively retrieve 25 PCLBCL-LT cases and 21 primary cutaneous follicle center lymphoma with large-cell morphology (PCFCL). To find clinical characteristics associated with MYD88 mutation in PCDLBCL-LT, to confirm its high prevalence, and to evaluate its prognosis impact, we conducted a retrospective multicentre study on 61 patients. Clinical features, treatment regimen and outcome were recorded. MYD88^{L265P} mutation was determined using real-time PCR analysis with Taqman allele specific probes.

RESULTS: Among 21 PCFCL, 2 (9.5%) were characterized by lower limb localization and 0/21 harbored *MYD88*^{L265P} mutation, which has been found in 19/25 (76%) of PCDLBCL-LT. Both specificity and positive predictive value were determined to be 100%, and negative predictive value was 78%.

To determine prognostic value, 61 patients diagnosed with PCLBCL-LT were included, and 34/58 (59%) patients harbored the *MYD88*^{L265P} mutation. Patients had similar clinical characteristics at presentation whatever their *MYD88* status, except age and tumour localization (older age and most frequent leg involvement in *MYD88* mutated group). There was no difference between both groups for treatment regimens. Considering overall survival, in univariate and multivariate analysis, *MYD88* mutation was an independent adverse prognostic factor, even after age adjustment (OR=2.94; 95%CI [1.185-7.295]; p=0.02).

CONCLUSIONS: We confirms the high prevalence of MYD88^{L265P} mutation in PCLBCL-LT, its diagnostic value among primary cutaneous large B-cell lymphomas and shows its association with shorter survival.

H-05 PRIMARY CUTANEOUS B-CELL LYMPHOMA – SYSTEMIC SPREAD IS RARE WHILST CUTANEOUS RELAPSES AND SECONDARY MALIGNANCIES ARE FREQUENT

ORAL Chan SA*1, Shah F, Chiganti S1, Stevens A1, Amel-Kashipaz R1, Vydianth B1, Scarisbrick JJ1

¹University Hospital Birmingham, United Kingdom

INTRODUCTION: Primary cutaneous B-cell lymphomas (CBCL) are rare lymphomas with an estimated annual incidence of 2-2.5 per 1,000,000 persons. They are classified as marginal zone lymphoma (MZL), follicular lymphoma (FCC) or diffuse large B-cell lymphoma (DLBCL) depending on the immunohistochemical phenotype of the malignant B-cells. The management and prognosis varies



Scientific Session H. Cutaneous B-cell Lymphomas

between these subtypes.

This is a cohort study of patients with primary CBCL from the University Hospital Birmingham (UHB) Specialist Cutaneous Lymphoma Service reporting demographics, staging, treatment and outcomes of patients treated and a metanalysis of the published literature. METHODS: All patients diagnosed with primary CBCL were identified from our cutaneous lymphoma database. Patients were classified according to ISCL-EORTC criteria. The clinical, pathological, management and outcomes of patients were recorded. Published studies of CBCL patients were reviewed and a meta-analysis undertaken.

RESULTS: 51 patients were included in this study including MZL n=21, FCC n=20 and DLBCL n=10. Patients with MZL and FCC were diagnosed at a younger age compared to patients with DLBCL with a median age of 47, 59 and 70.5. T classification at diagnosis ranged from T1a – T3. There was no correlation between T stage and outcome. Five-year disease specific survival (DSS) was 100% for MZL, 95% for FCC and 60% for DLBCL. Treatments for MZL and FCC include skin directed therapies such as excision and radiotherapy for localised disease with systemic therapies for more advanced disease. Patients with DLBCL mostly required first line systemic treatments. 13/51 (25.5%) had a second malignancy reported. Four hundred and thirty-three patients from 4 studies were identified for a meta-analysis. This included MZL (n=124), FCC (n=210) and DLBCL (n=99). The 5-year disease specific survival was 98.75% for MZL, 94.83% for FCC and 50.29% for DLBCL.

CONCLUSIONS: This cohort study and literature review confirms good prognosis for both MZL and FCC following first line skin directed therapy. However although systemic spread is rare cutaneous relapses are frequent (34%). Conversely DLBCL has a poor prognosis and requires first line systemic therapy. Staging lymphomas is typically used to stratify patients for prognosis and deciding treatment, however we did not find a difference between the T classification at diagnosis (T1 vs T2-3) and rate of recurrences, systemic spread or survival. We identified a high rate of second malignancies (mainly lymphoma/leukaemias and skin cancers) in our cohort 25.5% which has not previously been reported. Prospectively studying prognostic factors in CBCL would improve TNM classification with the aim of identifying patients at risk of recurrences /progression requiring more aggressive therapies.

H-06 PATCH AND THIN PLAQUE-TYPE LOW-GRADE PRIMARY CUTANEOUS B-CELL LYMPHOMA

POSTER Barzilai A*1,4, Amitay-Laish I^{2,4}, Didkovsky Y^{3,4}, Hodak E^{2,4}

¹Department of Dermatology, Sheba Medical Center, Tel Hashomer; ²Department of Dermatology and ³Institute of Pathology, Rabin Medical Center - Beilinson Hospital, Petach Tikva; and ⁴Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

INTRODUCTION: The low-grade primary cutaneous B-cell lymphomas (PCBCLs) usually present with erythematous infiltrated plaques, nodules, and tumors. We describe a new clinical variant of low-grade PCBCL characterized by patches and /or thin non-in-filtrated plaques.

METHODS: A retrospective study in which we reviewed the files of patients with low-grade PCBCL manifested by patches and/or non-infiltrated plaques attending the cutaneous lymphoma clinics of 2 referral medical centers in Israel between 2005 and 2015. RESULTS: Ten patients were identified: 8 male and 2 female, aged 16-67 years at diagnosis. Nine patients had erythematous non-scaly patches, some with annular/reticular configuration, and 3 had erythematous thin non-infiltrated plaques, with/without patches. In 2 patients, only patches (1) and or patches and thin plaques (1) were observed, whereas in the other 8, infiltrated plaques or nodules appeared before, concomitant with, or after the macular lesions. No predilection for a specific location was noted. The clinical differential diagnosis included a vascular lesion, figurate erythema, interstitial mycosis fungoides, and macular form of granuloma annulare. Histologic study of the macule/non-infiltrated plaques showed either superficial and deep perivascular and/or periadnexal moderately dense lymphocytic infiltrates or small nodular aggregates located mainly in the superficial dermis. The combination of the histopathologic and immunohistochemical findings led to the diagnosis of follicular center cell lymphoma in 5 patients and marginal zone lymphoma in 4 patients. In one patient, the exact subtype of the low-grade B cell lymphoma could not be determined. CONCLUSIONS: Low-grade PCBCL can present with patches/non-infiltrated plaques, either as the sole manifestation or concomitant with the more classic lesions of the lymphoma. This unique presentation poses a diagnostic challenge and clinicians and pathologists should be alert to it.

H-07 METHOTREXATE-INDUCED B-CELL CUTANEOUS LYMPHOMA IN ERYTHRODERMIC CUTANEOUS T-CELL LYMPHO-MA PATIENTS

POSTER Delaleu J¹, Marc S¹, Levy A², Guyot A¹, Maubec E¹, Dereure O³, Laroche L*¹

¹Assistance Publique des Hôpitaux de Paris (APHP), Hôpital Avicenne, Dermatology Department, University of Paris 13, Bobigny, France; ²APHP, Hôpital Avicenne, Pathology Department, AP-HP, Bobigny, France; ³Hôpital de Montpellier, Dermatology Department, University of Montpellier, Montpellier, France

We report a series of 3 cases of B-cell lymphoma (CBCL) occurring in erythrodermic cutaneous T-cell lymphoma (CTCL) patients treated with methotrexate (MTX). A 80-year-old woman with erythrodermic Mycosis Fungoides (MF) in partial remission after 10 months of MTX presented with a single ulcerated nodule. Histology showed a large-cell CD20+ EBV+ CBCL associated with underlying MF. The nodule disappeared one month after MTX discontinuation, without relapse at 3.3 years. A 78-year-old man with Sezary syndrome (SS) developed 5 isolated ulcerated nodules 20 months after starting MTX. Biopsy revealed a diffuse large-cell CD20+ EBV+ CBCL. Nodules resolved after 2.5 months of MTX discontinuation associated with bexatorene, extracorporeal photochemotherapy (ECP) and topical steroids, without relapse at 3.5 years. A 64-year-old woman with SS was treated with MTX alone followed by association with bexatorene and ECP. 66 months later, a severe skin and nodal relapse occurred. Skin biopsies

Scientific Session H. Cutaneous B-cell Lymphomas

disclosed a massive lymphocytic infiltrate combining SS pattern and a large-cell CD20+ EBV- CBCL. Lymph node biopsy revealed SS involvement. All nodules disappeared after 6 months of MTX discontinuation in association with R-CHOP, while SS relapsed at 3 months. Most MTX-induced CBCL have been reported in rheumatoid arthritis, 50% of them being extranodal, with a late onset (median of 58 months) and EBV expression in 50% of cases. Remission after MTX discontinuation amounts to 55%. Only 3 cases of MTX induced-CBCL have been described in patients with CTCL (2 SS and 1 MF), all being EBV+ and resolving after MTX cessation, often associated with rituximab administration. This is the first series of CBCL in patients treated with MTX for eCTCL presenting with ulcerated nodules. In one case, CBCL and CTCL cells were intertwingled in skin biopsies. One case was EBV-, which had never been described before. Lesions disappeared in less than 3 months after MTX discontinuation alone (n=1), or in association with other drugs (n=2). No CBCL relapse was observed. Onset of tumor(s) in CTCL patients treated with MTX should bring to mind the possibility of MTX- induced CBCL, especially when CTCL is otherwise well-controlled.

H-08 RITUXIMAB MONOTHERAPY FOR PRIMARY CUTANEOUS B-CELL LYMPHOMA: RESPONSE AND LONG-TERM FOL-LOW-UP IN 24 PATIENTS

POSTER Jonak C*, Paniec P, Porkert S, Valencak J Department of Dermatology, Medical University of Vienna, Austria

INTRODUCTION: Primary cutaneous B-cell lymphomas (CBCL) are cutaneous lymphomas (CLs) with a B-cell phenotype, comprising about 25% to 29% of all primary CLs. Since more than a decade, the monoclonal anti-CD20 antibody rituximab has been approved for treatment of follicle center lymphoma (FCL) and marginal zone lymphoma (MZL), representing the most common CBCL variants. Aim of this study was to evaluate the long-term therapeutic value of rituximab in 24 CBCL patients.

METHODS: In this retrospective study, all included patients were diagnosed and treated at the Department of Dermatology, Medical University of Vienna. Patients received systemic treatment of rituximab 375mg/m² once weekly. Number of recurrences and duration of therapeutic response were evaluated and compared with previously published literature. RESULTS: Our study-population consisted of 8 patients with MZL and 16 with FCL. Following intravenous therapy with rituximab, 75% of patients showed a complete response and 25% a partial remission. A recurrence rate of 52 % was observed. The median time to recurrence was 18 months. The mean observation period was 88 months. No severe side effects were observed.

CONCLUSIONS: Results indicate a high rate of durable remissions and even patients with relapses responded well to treatment. In CBCL, the choice of therapy is limited to skin-directed therapies, such as surgery or radiotherapy in case of solitary lesions. On basis of our results, single-agent treatment with anti-CD20 antibody rituximab still remains to be feasible and safe in CD20 positive B-cell lymphomas.

H-09 MALIGNANT ROSACEA AS A SIGN OF SYSTEMIC MARGINAL ZONE LYMPHOMA

POSTER Lamoureux A¹, Vergier B^{2,3}, Milpied N⁴, Beylot-Barry M*^{1,3}

¹Dermatology Department, CHU Bordeaux, Bordeaux, France; ²Pathology Department, CHU Bordeaux, Bordeaux, France; ³INSERM U1053,Bordeaux research in Translational Oncology, Team 3 oncogenesis of cutaneous lymphomas, Univ. Bordeaux, France; ⁴Hematology Departement, CHU Bordeaux, Bordeaux, France

Rosacea is a common facial dermatosis for which differential diagnoses have to be considered in the case of atypical features or treatment failure. We report 3 cases of systemic marginal zone lymphoma (MZL) with skin involvement simulating rosacea. A 76-year-old man presented a rhinophyma for one year. Due to micropapular purplish aspect, the diagnostic was challenged and a biopsy was performed to exclude an angiosarcoma. Biopsy showed a dense infiltrate of small B-cells corresponding to MZL. Staging revealed lomboaortic lymph-nodes and a medullar involvement. Polychemotherapy associated with rituximab allowed remission. A 75-year-old woman had a one year history of untreated systemic MZL (splenomegaly and moderate hyperlymphocytosis 4000/ mm3). She was referred for a facial dermatosis considered as rosacea for many months. She presented multiple pink micropapules without pustules. Biopsy confirmed skin involvement of MZL. An identical B-cell clone was found in the skin and blood. Polychemotherapy with fludarabine and cyclophosphamide allowed remission, but 3 years later, transformation into a large B-cell lymphoma of the cavum led to a fatal outcome. A 75-year-old female, with a one year medical history of hyperlymphocytosis (10000/mm3) was referred after the excision of a nodule of the arm corresponding to a MZL. Clinical examination revealed an erythema of lower eyelids, pink micropapules of forehead and scalp and a cervical lymphadenopathy. Skin and nodal biopsies concluded to a MZL with an identical B-cell clone in the skin, node and blood. A treatment by rituximab was begun. Primary cutaneous MZL classically appears as isolated or multiples nodules of the trunk and limbs, and less frequently the face. We reported a different and quite stereotyped clinical picture in our 3 patients. This rare clinical picture mimicking rosacea has been reported in isolated case reports and in one series from Barzilai et al. of primary cutaneous B-cell lymphoma (mainly MZL but also follicle center lymphoma). To our knowledge, only one case has been reported of such presentation revealing systemic MZL. Lastly, none of our patients had preexisting flush or telangiectasia as opposed to some of those reported by Barzilai.

Scientific Session H. Cutaneous B-cell Lymphomas

H-10 PRIMARY CUTANEOUS FOLLICULAR B CELL LYMPHOMA OF THE SCALP ASSOCIATED WITH ANDROGENETIC ALO-PECIA IN MEN.

POSTER Martinez-Escala E, Yelamos O, Amin SM, Guitart J* Northwestern University Dept. of Dermatology Chicago IL

We have observed a high prevalence of men with limited scalp involvement among our patients with primary cutaneous follicular B cell lymphoma of the skin (PCFL) This is a retrospective review of patients diagnosed with primary cutaneous follicular B-cell lymphoma at our institution from 2006 to 2016. Clinical data and skin biopsies of all eligible patients were collected and reviewed. We identified 52 of 87 PCFL patients in our database had scalp involvement. We were able to evaluate 48 of these patients for the presence of androgenetic alopecia (AA), 30 of whom were noted to have AA (26M, 4F). This group had a median age of 54 years (31-82), slightly younger than the entire PCFCL group of 56.5. Most of these patients had limited and localized disease (T1=17, T2=7, T3=2) and most patients achieved a complete response (13/17) with skin directed therapies (surgery, IL steroids or radiation). Only one patient had nodal involvement and splenomegaly, which resolved with systemic therapy. Skin biopsies showed a predominance of a nodular pattern (21/26) with a mixture of centrocytes and centroblasts, while a diffuse pattern with large cells was noted on 5/26. None of these patients with AA had disease progression with a median f/u of 38 months (2-19 years). PCFCL is significantly associated with scalp involvement and androgenetic alopecia in men (p=0.01. This presentation tends to be indolent with no evidence of disease progression in any of our cases.

H-11 T-CELL PAPULOSIS ASSOCIATED WITH B-CELL MALIGNANCY: A DISTINCTIVE CLINICOPATHOLOGIC ENTITY

POSTER Visseaux L¹, Beylot-Barry M^{*2}, Durlach A³, Barete S⁴, Bayaram M³, Bonnet N⁵, Chassine AF⁶, Combemale P⁷, Dhaille F⁸, Franck N⁹, Herve G¹⁰, Leclec'h C¹¹, Machet L¹², Ingen-Housz-Oro S¹³, Petrella T¹⁴, Vergier B¹⁵, Ortonne N¹⁶, Grange F¹, and the-French Study Group on cutaneous lymphomas (GFELC)

¹Dermatology, Reims University Hospital; ²Dermatology, Bordeaux University Hospital; ³Pathology, Reims University Hospital, ⁴Dermatology, AP-HP, La Pitié-Salpêtrière University Hospital, Paris; ⁵Dermatology, Cochin Hospital, Paris; ⁶Dermatology, Prouzel; ⁷Oncodermatology, Léon Bérard Center, Lyon; ⁸Dermatology, Amiens University Hospital; ⁹Dermatology, Cochin Hospital, Paris; ¹⁰Pathology, AP-HP, La Pitié-Salpêtrière Hospital, Paris; ¹¹Dermatology, Angers University Hospital; ¹²Dermatology, Tours University Hospital; ¹³Dermatology, AP-HP, Henri Mondor University Hospital, Créteil; ¹⁴Pathology, Dijon University Hospital; ¹⁵Pathology, Bordeaux University Hospital; ¹⁶Pathology, Henri Mondor University Hospital, Créteil.

INTRODUCTION: A distinctive eruption consisting in chronic and recurrent papules sometimes associated with papulo-vesicles and/ or nodules, often occurs during the course of hematological B-cell malignancies (BCM) although its clinical evolution, histopathological features and pathogenesis remain unclear. We sought to describe the clinical and histopathological characteristics of this eruption and to investigate its pathogenesis and possible relationship with the underlying BCM.

METHODS: Multicenter, retrospective study of patients aged > 18 years with a BCM and a cutaneous eruption consisting in chronic and/or recurrent papules, papulo-vesicles and/or nodules. The following items were assessed: clinical, histopathological, immuno-histochemical and molecular data.

RESULTS: Thirty-seven patients were included. No significant insect bite history or seasonal predominance was recorded. Clinical lesions were pruritic papules (81%), papulo-vesicles (43%) and nodules (38%) and had a chronic course, without complete remission periods in most cases (57%). The associated BCM was a chronic lymphocytic leukemia in most cases (73%). The histological and immunohistochemical review showed: a dense dermal lymphocytic infiltrate predominantly composed of T lymphocytes (100%), with frequent eosinophils (77.6%); a perivascular and periadnexial (most often pilotropic) pattern (77.6%), sometimes suggestive of a pilotropic mycosis fungoides. Clusters of tumor B-cells were identified in 47% of cases. In 10/14 cases (71.4%) tested for B-cell IgH gene rearrangement, a B-cell clone was identified in skin lesions (identical to the blood one in 9 cases), whereas no T-cell clone was present.

CONCLUSIONS: We propose the denomination "T-cell papulosis associated with B-cell malignancy" (TCP-BCM) for this distinctive cutaneous entity previously considered as an insect-bite reaction. Although resulting in various histopathological pictures, this eruption can be easily recognized by clinicians, and may be identified by informed pathologists relying on some key features. An extravasation of tumor B-cells with skin-homing properties associated with a secondary, predominant, T-cell immune reaction could explain the clinico-pathologic aspect, as well as the prolonged regressive and recurrent course of the disease.

* indicates presenting author

Scientific Session I. Rare Cutaneous Lymphomas

I-01 A NEW LOOK AT ATOPY IN CD30+ CUTANEOUS LYMPHOPROLIFERATIVE Disorders

ORAL Kadin ME1*, Vonderheid EC2

¹Boston University and Roger Williams Medical Center, Providence RI; ²Johns Hopkins Medical Institute, Baltimore MD, USA

INTRODUCTION: Previous epidemiologic studies indicated an increased prevalence of atopic disorders (atopic dermatitis, hay fever/allergic rhinitis, asthma) in patients with primary cutaneous CD30+ lymphoproliferative disease (CD30LPD). Our aim was to further clarify the relationship between atopy, lymphomatoid papulosis (LyP) and primary cutaneous anaplastic large cell lymphoma (pcALCL).

METHODS: We performed a retrospective review of medical records of 155 patients with LyP and 22 patients with pcALCL for history of atopic disorders. We quantified serum IgE and eosinophils in most patients. Because IL-13 is associated with atopy, we examined IL-13 secretion by pcALCL lines and its expression in skin lesions.

RESULTS: LyP patients had a lower lifetime prevalence of allergic rhinitis/hay fever (29.0%) than controls (38.2%, P= 0.022). This difference was found for LyP-A but not LyP-C. Although a history of eczema was not significantly different for all LyP patients, it was higher for LyP-C patients (8 of 36 or 22%) than published controls (7.21%, P= 0.004). Patients with pcALCL had a decreased prevalence of allergic rhinitis/hay fever compared with controls (P= 0.006). The risk of penicillin allergy for patients with pcALCL was higher than expected (P= 0.009).

Mean levels of total IgE for patients with LyP (188.8 kU/L) and pcALCL (164.0 kU/L) were significantly higher than reported for the American population (P< 0.001). IgE levels > 100 kU/L occurred in 35 of 117 (29.9%) LyP patients overall, (37% of LyP-C) and 5 of 14 (36%) pcALCL patients. Blood eosinophil counts in LyP and pcALCL patients were not significantly different than the American population (P= 0.502). However, eosinophils surrounded IL-13+ tumor cells in skin lesions. CD30+ cells in pcALCL lines and clinical samples contained both IL-13 and Th17 cytokines, similar to a novel subset of CD4+ Th2/Th17 memory effector T cells that promote chronic allergic asthma (J Exp Med 207:2479), suggesting a cellular link of CD30LPD to atopy.

CONCLUSIONS: Our study provides biochemical evidence (increased serum IgE) suggesting that atopy may underly the pathogenesis of CD30LPD. Further analysis that takes into account the effect of age, race and gender on IgE levels is planned. The finding of CD30+ cells co-producing IL-13 and Th17 cytokines provides new evidence linking CD30LPD to atopy.

I-02 TOX EXPRESSION IN CUTANEOUS T-CELL LYMPHOMAS AND CUTANEOUS B-CELL LYMPHOMAS

ORAL Schrader AM*, Jansen PM, Willemze R

Dept. of Pathology and Dept. of Dermatology, Leiden University Medical Center, Leiden, The Netherlands

INTRODUCTION: TOX, associated with development of CD4⁺ T-cells in the thymus, was shown to be aberrantly expressed in CD4⁺CD8⁻ neoplastic T-cells in mycosis fungoides (MF) and Sézary syndrome (SS), but not or rarely by skin-infiltrating T-cells in benign inflammatory dermatoses (BID). Data on expression in other types of cutaneous T-cell lymphoma (CTCL) and cutaneous B-cell lymphoma (CBCL) are scarce, and it is unknown whether TOX can be expressed by CTCL with phenotypes other than CD4⁺CD8⁻. METHODS: Immunohistochemical expression of TOX was evaluated in 132 patients with various types of CTCL with different T-cell

phenotypes, and in 44 patients various types of primary and secondary CBCL, selected from the Cutaneous Lymphoma Registry of the Leiden University Medical Center, Leiden, The Netherlands. Expression in > 50% of the tumor cells was considered positive. RESULTS: TOX was strongly expressed in 49/59 patients (83%) with MF and 19/22 patients (86%) with SS, but also variably by other types of CTCL, and by CTCL with phenotypes other than CD4⁺CD8⁻. Although only 1/60 BID patients (2%) expressed TOX in > 50% of the skin-infiltrating T-cells, the majority of BIDs had expression varying between 11% and 50%. Unexpectedly, TOX was also expressed by follicle center cells in reactive lymph nodes and tonsils, by neoplastic follicle center cells in 16/17 patients (94%) with primary cutaneous follicle center cell lymphoma, 7/7 patients (100%) with secondary skin manifestations of follicular lymphoma, and by the neoplastic B-cells in 4/13 patients (31%) with primary cutaneous diffuse large B-cell lymphoma, leg type and 2/2 patients (100%) with secondary skin manifestations of diffuse large B-cell lymphoma.

CONCLUSIONS: TOX expression in CTCL is not tumor-specific, is not restricted to the CD4⁺CD8⁻ phenotype, and, on its own, is insufficient for diagnosis. Besides expression in T-cells, TOX also is expressed by both reactive and neoplastic follicle center B-cells and a proportion of neoplastic B-cells in primary and secondary cutaneous diffuse large B-cell lymphoma of which the functional significance remains to be elucidated.

Scientific Session I. Rare Cutaneous Lymphomas

I-03 NO TP63 REARRANGEMENTS IN A SELECTED GROUP OF PRIMARY CUTANEOUS CD30+ LYMPHOPROLIFERATIVE DISORDERS WITH AGGRESSIVE CLINICAL COURSE

ORAL Schrader AM*¹, Chung YY², Jansen PM¹, Szuhai K³, Bastidas Torres AN², Tensen CP², Willemze R²

¹Department of Pathology, ²Department of Dermatology, and ³Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, The Netherlands.

INTRODUCTION: CD30⁺ lymphoproliferative disorders (CD30⁺ LPDs), including primary cutaneous anaplastic large cell lymphoma (C-ALCL) and lymphomatoid papulosis (LyP), have an excellent prognosis, however, about 10% run an aggressive clinical course for which risk factors are currently unknown. In systemic anaplastic large cell lymphoma without ALK rearrangements (ALK- ALCL), rearrangements in the TP63 gene were associated with a poorer overall survival, and therefore, the presence of TP63 rearrangements was studied in a selected group of CD30⁺ LPDs with aggressive clinical course.

METHODS: Immunohistochemistry for p63 and fluorescence in situ hybridization (FISH) with break-apart probes for TP63 were performed on formalin-fixed and paraffin-embedded biopsy specimens of 14 patients with C-ALCL and three patients with LyP that were selected for their aggressive clinical course from the Cutaneous Lymphoma Registry of the Leiden University Medical Center, Leiden, The Netherlands.

RESULTS: Immunohistochemistry for p63 was positive in more than 30% of the tumor cells in 6/17 patients (35%) and no expression was seen in 7/17 patients (41%). In none of the 17 patients, a genetic rearrangement of the TP63 gene was detected by FISH analysis.

CONCLUSIONS: This study suggests that in patients with CD30⁺ LPDs, an aggressive clinical course cannot be defined by the presence of TP63 rearrangements, as was recently shown in systemic ALK- ALCL. In addition, immunohistochemical expression of p63 is variable in CD30⁺ LPDs and not related with overall survival.

I-04 SKIN MANIFESTATIONS AND OUTCOME IN ADULTS WITH PRE-B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA; AN IMPORTANT DIFFERENTIAL DIAGNOSIS TO PRIMARY CUTANEOUS FOLLICLE CENTER LYMPHOMA, DIFFUSE TYPE AND SECONDARY CUTANEOUS FOLLICULAR LYMPHOMA

ORAL Flores-Bozo LR¹, Demichelis-Gómez R², Inclan-Alarcon S², Pomerantz A², Rodríguez-Rodríguez S², Montante-Montes de Oca D³, Lome-Maldonado C⁵, Charli-Joseph Y^{*1,4}

¹Departments of Dermatology, ²Hematology, ³Pathology and ⁴Cutaneous Hematopathology Clinic, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City and ⁵Division of Pathology, Instituto Nacional de Cancerología, Mexico City, Mexico.

INTRODUCTION: Leukemia cutis (LC) secondary to acute lymphoid leukemia (ALL), particularly Pre-B-ALL, is rare in adults; existing only two reports. Herein we describe the clinical, histopathological, immunophenotypic and molecular features of adults with Pre-B-ALL-LC and analyze potential prognostic factors and survival as compared to a cohort of Pre-B-ALL adults without LC.

METHODS: Six adults with Pre-B-ALL-LC were identified in our cohort of 173 adults over a 25-year period (3.4%). Dermatological characteristics were retrieved along with information on stage, immunophenotype, treatment, outcome and survival. All pathological specimens (cutaneous and extra-cutaneous) were analysed. Recovered information was compared with that of Pre-B-ALL adults without LC.

RESULTS: Pre-B-ALL-LC occurred in 2 women and 4 men, aged 20-70 years (mean 43), in an average of 6.1 months after diagnosis of Pre-B-ALL. Lesions were multiple (83.3%), occurred on the scalp (100%), face (50%), neck (16%) and/or trunk (16%), and consisted of erythematous nodules (83.3%) and infiltrated plaques (50%). Histopathological sections showed predominantly angiocentric (65%), dermal and subcutaneous (100%) infiltrates of medium-sized blast-like cells; with a CD10+ (6/6), CD20+ (5/6), CD79+ (3/3), PAX5+ (2/2), TdT+ (5/5), CD34- (5/5) immunophenotype. Average survival was statistically similar amongst patients with Pre-B-ALL-LC (17 months) and those without LC (9 months). Prevalence of non-cutaneous extramedullary disease was 33% in LC cases, 21% amongst the cohort. 50% of Pre-B-ALL-LC cases displayed a 9:22 translocation, 11.4% in those without LC (p0.02).

CONCLUSIONS: These study reports the main features of the first series of pre-B-LAL-LC in adults. Average age, clinical features and histomorphology were similar to those of non-pre-B-LC, excepting a stark predilection for scalp involvement. Karyotypic aberrations (t9:22) were statistically more frequent in Pre-B-ALL-LC than in Pre-B-ALL adults without LC, and could signify a risk factor for cutaneous dissemination; surprisingly, the former showed a slight tendency for improved survival compared to the latter, contrary to the dismal prognosis reported for non-pre-B-LC. In conclusion, Pre-B-ALL-LC is exceptional in adults but should be recognized in the differential diagnosis of rapidly growing nodules or plaques, and a comprehensive knowledge of it's typical histopathological and immunophenotypic features is essential for it's distinction with other B-cell neoplasms that more commonly involve the skin.

Scientific Session I. Rare Cutaneous Lymphomas

I-05 CUTANEOUS MANIFESTATIONS OF ADULT T-CELL LYMPHOMA/LEUKEMIA. MONOCENTRIC STUDY OF 37 PATIENTS BETWEEN 1996 AND 2016

ORAL Hurabielle C^{*1}, Battistella M², Ram-Wolff C¹, Fite C³, Meignin V², Rivet J², Vignon-Pennamen MD², Raffoux E⁴, Arnulf B⁴, Oksenhendler E⁴, Sicre de Fontbrune F⁵, Peffault de Latour R⁵, Sicard H⁶, Socié G⁵, Bouaziz JD¹, Lebbé C¹, Bagot M¹

¹Dermatology, Saint-Louis Hospital, AP-HP, Paris, France; ²Pathology, Saint-Louis Hospital, AP-HP, Paris, France; ³Dermatology, Bichat Hospital, AP-HP, Paris, France; ⁴Clinical Immunology, Saint-Louis Hospital, AP-HP, Paris, France; ⁵Hematology Transplantation, Saint-Louis Hospital, AP-HP, Paris, France; ⁶Innate Pharma, Marseille, France

INTRODUCTION: Adult T-cell lymphoma/leukemia (ATLL) is a hematologic malignancy associated with chronic infection by HTLV-1. HTLV-1 infection is endemic in Japan, Central and South America, subtropical Africa and the Caribbean, where about 5% of the infected patients develop ATLL. Cutaneous manifestations are variable, categorized in patches, plaques that are often arc-shaped, multipapular, nodulotumoral, erythrodermic and purpuric types. We report all the cases of ATLL with cutaneous localization diagnosed in our centre for the past 20 years.

METHODS: All the patients diagnosed with ATLL in our centre between 1996 and 2016 were included. We collected clinical features such as the presence and if so type of cutaneous manifestation, treatments, and histologic features.

RESULTS: 37 patients diagnosed for ATLL were included. Among them, 15 patients (41%) had a cutaneous localization of the disease, which was present from the beginning of the disease for two thirds of them, and even revealed the disease for 6 of them. Only one came from Metropolitan France and had probably been infected with the HTLV-1 after a blood transfusion. Cutaneous localization observed were as follow (half the patients had 2 or more cutaneous manifestations): nodulotumoral (n=8), plaques (n=7), multipapular (n=6), patches (n=4), purpuric (n=2).

Skin histologic findings consisted in medium to large-size CD4⁺CD25⁺ T-cells with flower-shaped nuclei. In the 3 last cases, we performed KIR3DL2 immunostaining on frozen skin biopsies and we observed 1.4%, 13.5% and 25% of KIR3DL2⁺ malignant T-cells respectively. In smoldering and chronic forms, interferon possibly associated with antiretroviral therapies, PUVA therapy or caryolysine were used to treat the disease whereas in lymphoma and acute forms, the treatment was more aggressive, with polychemotherapies and bone marrow transplantation.

CONCLUSIONS: ATLL is a hematologic malignancy with variable expression that is exceptionally diagnosed in France, but should be mentioned in patients coming from countries with high HTLV-1 prevalence. Chronic and smoldering types are relatively indolent, whereas acute and lymphoma forms have remarkably poor prognosis. KIR3DL2 expression by tumour cells may however represent an attractive therapeutic target in the future.

I-06 BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM: AN UPDATE ON CYTOGENETIC DATA

ORAL Corti L¹, Fanoni D¹, Venegoni L², Merlo V¹, Alberti-Violetti S^{1*}, Berti E²

¹U.O.C. Dermatologia – Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan (Italy); ²Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti - Università degli Studi di Milano, Milan (Italy)

INTRODUCTION: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive hematologic disease characterized by skin lesions and a simultaneous or subsequent involvement of peripheral blood, bone marrow and lymph nodes. The aims of our study were to update our previous genomic analysis on BPDCN and to better investigate cases with an acute leukemic spread. METHODS:

We collected 26 cases of BPDCN and analyzed clinico-pathological, immunophenotypical and molecular data. Molecular analysis were performed using array-CGH on frozen DNA samples. RESULTS: In our cohort, median age at diagnosis was 59 years (range 9 - 83) with a median overall-survival (OS) of 22 months: 17 patients died from the disease, 2 patients died from the therapy, and another death was not disease related. Four dead patients had an acute leukemic spread. At the last follow-up time 6 patients were alive, and 3 disease free. All cases had typical PDC immunophenotype. CD4 and/or CD56 were lost in 3 of them and aberrant expression of CD2 and/or CD7 were seen in 9/26. Neoplastic cells from one patient with leukemic spread were unexpectedly positive for membrane CD3 and PD-I (CD279). Genomic analysis confirmed previously described alterations, with losses on chromosomes 9 (up to 73% of cases), 13 (62%), 12 (50%), and 7 (23%). Interestingly, all patients with leukemic spread showed an uncommon loss on chromosome 1p31.2. Furthermore these patients presented the same genomic profile in both skin and peripheral blood samples. CONCLUSIONS: Molecular analysis confirmed that BPDCN is characterized by a pattern of several genomic losses, involving multiple cell cycle checkpoints. The results, in fact, confirmed the prevalent involvement of regions located on chromosome 9, 12 and 13, which harbour genes involved in cell cycle progression or tumor suppression. The region lost on chromosome 1 in the leukemic group deserves to be better investigated.

Scientific Session I. Rare Cutaneous Lymphomas

I-07 EXPRESSION OF TFH MARKERS AND DETECTION OF RHOA P.G17V AND IDH2 P.R172K/S MUTATIONS IN CUTANE-OUS LOCALIZATIONS OF ANGIOIMMUNOBLASTIC T-CELL LYMPHOMAS

ORAL Alirkilicarslan AL¹, Dupuy A^{*2,3}, Pujals A^{1,2,3}, Parrens M⁴, Vergier B⁴, Robson A⁵, Delfau-Larue MH^{2,3,6}, Oro S⁷, Chosidow O⁷, Haioun C^{2,3,8}, Beylot-Barry M⁹, Merlio JP^{10,11}, Copie-Bergman C^{1,2,3}, Gaulard P^{1,2,3}, Ortonne N^{* 1,2,3}

¹Département de Pathologie, Groupe Henri-Mondor, Assistance Publique – Hôpitaux de Paris, Créteil, France. ²INSERM U955 équipe 9, Institut Mondor de Recherche Biomédicale, Créteil, France. ³Université Paris Est, Créteil, France. ⁴Service d'Anatomie et Cytologie Pathologiques Sud, hôpital Haut-Lévêque, CHU de Bordeaux, 33604 Pessac, France. ⁵Departamento de Diagnóstico Laboratorial IPOLFG - Serviço de Anatomia Patológica Rua Prof Lima Basto, 1099-023 Lisboa, Portugal. ⁶Département d'Immunologie Biologique, Groupe Henri-Mondor, Assistance Publique – Hôpitaux de Paris, Créteil, France. ⁷Service de Dermatologie, Groupe Henri-Mondor, Assistance Publique – Hôpitaux de Paris, Créteil, France. ⁸Unité Hémopathies Lymphoides, Groupe Henri-Mondor, Assistance Publique – Hôpitaux de Paris, Créteil, France. ⁹Service de Dermatologie, Haut-Lévêque Hospital, CHU de Bordeaux, 33604 Pessac, France. ¹⁰INSERM U1053 Bordeaux Research in Translational Oncology Université de Bordeaux. ¹¹Service de Biologie des Tumeurs, Hôpital Haut-Lévêque, CHU de Bordeaux, 33604 Pessac, France.

INTRODUCTION: There are few studies on skin manifestations of angioimmunoblastic T-cell lymphomas (AITL), in particular those on the expression of follicular helper CD4⁺ T cell (TFH)-associated markers. The presence of recently reported recurrent mutations of IDH2 and RHOA genes in AITL has not yet been studied in skin infiltrates of AITL patients.

METHODS: We retrospectively analyzed 41 skin biopsies for the expression of B, T, and TFH markers, as well as the presence of EBV by in situ hybridization, and the presence of RHOA (p.G17V) and IDH2 (p.R172K/S) mutations using allele-specific PCR.

RESULTS: We categorized cases into three distinctive patterns based on their pathology: 1) low-density lymphocytic perivascular infiltrates (n = 11), 2) atypical dense and compact perivascular infiltrates, sometimes with a granulomatous reaction pattern (n = 13), or 3) diffuse infiltrates reminiscent of AITL (n = 4). Unusual features, including EBV-positive lymphoproliferative disorder or plasmocytoid B-cell components were seen in 13 cases. We observed the loss of CD7 in 42% of cases, the expression of TFH markers (CD10 (50%), BCL6 (84%), PD1 (94%), CXCL13 (84%), and ICOS (97,5%)), and EBV⁺ B-blasts in 26% of cases. A TFH phenotype was identified in most cases, particularly in 82% and 73% of cases with the most challenging patterns (patterns 1 and 2). We found RHOA and IDH2 mutations in the skin samples of 14/18 (78%) and 2/16 (12%) cases, respectively. The RHOA mutation was detected both in the skin and lymph node biopsies in 7/11 (64%) cases, and in only the skin or the lymph node of one sample each.

CONCLUSIONS: The morphological features of skin lesions of AITL are highly variable. Expression of TFH markers by neoplastic T-cells in the skin is seen in most cases. The frequency of RHOA mutations in AITL skin lesions appears to be similar to that reported in lymph nodes. The identification of RHOA mutations in skin lesions may represent a new diagnostic tool.

I-08 A single-centre experience of 9 patients diagnosed with blastic plasmacytoid dendritic cell neoplasm during a 5-year-period

POSTER Estrach T^{1*}, Baliu-Piqué C¹, Mozas P², Baumann T², Velásquez C², García A³, Rovira M², Villamor N⁴, Colomer D⁴, López Guillermo A², Esteve J²

Department of ¹Dermatology, ²Haematology, ³Pathology and ⁴Haematopathology Unit, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain

INTRODUCTION: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare haematological malignancy with an aggressive clinical course. Diagnosis may be difficult, consensus on standard treatment is lacking and duration of chemotherapy response is short with poor long-term prognosis. Few case series are reported in the literature. We report on epidemiological, clinical and immunophenotypical features of our patients, as well as treatment outcomes

METHODS: A retrospective cohort study was conducted in a single tertiary hospital. 9 patients (6 men/3 women; median age: 49, range: 15-81) with BPDCN diagnosed between 2010 and 2015 were included. If feasible by patient's age and comorbidity, we administered high-risk acute lymphoblastic leukaemia (ALL)-type chemotherapy followed by allogeneic hematopoietic stem-cell transplantation (alloHCT).

RESULTS: Out of these 9 patients, 2 of them had a history of myelodysplastic syndrome. All except one had skin manifestations: 2 of them only had skin involvement; 5 out of 9 patients had lymphadenopathy and peripheral blood expression; 6 out of 9 patients had bone marrow infiltration, and 2 patients had manifestations in all the locations previously mentioned. Concerning the immunophenotype, all of them expressed CD4, CD56 and CD123; blood dendritic cell antigen 2 and 4 (BDCA-2 and 4) were positive in 8/9 of them. 7 patients were treated with ALL-type chemotherapy, followed by alloHCT in 5. Two elderly patients were treated with CHOP-type chemotherapy. The overall response rate was 88% (7/7 after ALL-type chemotherapy, 1/2 after CHOP). After a median follow-up of 60 months (6-96), 6 out of 7 patients treated with ALL-type chemotherapy remain in clinical remission, including all patients allografted, and the remaining patient presented a rapid relapse (11 months). On the contrary, two patients treated with CHOP-like regimen developed a rapid progression. Five-year survival is 66%.

CONCLUSIONS: Given the high prevalence of skin lesions in BPDCN and typical CD4 expression, diagnosis of BPDCN should be considered in presumptive skin lymphoma lesions based only in CD4 positivity. Referring to our outcomes, our patients were younger than ones reported in the literature.
* indicates presenting author

Scientific Session J. Quality of Life & Outcomes Studies

J-01 COST-EFFECTIVENESS ANALYSIS OF SYSTEMIC TREATMENTS FOR CUTANEOUS T-CELL LYMPHOMA

ORAL Geskin LJ*, Hines LE, Sharma V, Malone DC

Columbia University, Pharmacy Quality Alliance, Mallinckrodt Pharmaceuticals, University of Arizona

INTRODUCTION: New therapies have evolved over the past 15 for the treatment of cutaneous T-cell lymphoma (CTCL), a rare heterogeneous group of non-Hodgkin lymphomas. The purpose of this study was to conduct a cost-effectiveness analysis of systemic treatment options used for more advanced stages of CTCL.

METHODS: A cost-effectiveness model was constructed to compare systemic bexarotene, denileukin diftitox, interferon alfa, methotrexate, pralatrexate, romidepsin, vorinostat, and extracorporeal photopheresis (ECP) for CTCL. Data on the effectiveness for each treatment were extracted from published studies and US product labeling. The primary measure of effectiveness, overall response, was defined as the proportion of patients achieving either complete or partial response. Costs were based on wholesale acquisition cost for medications and Medicare reimbursement rates for ECP, medication administration, and treatments due to adverse drug effects. A survey of treating clinicians was used to determine current prescribing practices and length of treatment. The model was constructed using a payer perspective. Probabilistic sensitivity analysis was conducted using a Monte Carlo simulation. Beta distributions were used for probabilities in the model and gamma distributions were used for cost and utilization variables. A Monte Carlo simulation was conducted 1,000 times to estimate effects, cost, and cost-effectiveness.

RESULTS: The lowest cost option was methotrexate (mean \$426; standard deviation (SD) \$212), with the next lowest cost options being interferon alpha (mean \$2,503; SD \$2,835) and ECP (mean \$36,545; SD \$37,612). All other treatments had costs greater than \$40,000 ranging from \$44,741 (SD \$21,149) for denileukin diftitox to \$271,344 (SD \$215,860) for bexarotene. With respect to cost-effectiveness, all treatments were compared to methotrexate. The incremental cost-effectiveness ratio per successfully treated patient for interferon was \$21,704 and \$154,105 for ECP. Incremental cost per success for bexarotone was over \$3,400,000. For pralatrexate the incremental cost per success was over \$10 million. The treatments of denileukin diftitox, romidepsin, and vorinostat, were dominated (higher cost, less effective) by methotrexate.

CONCLUSIONS: Among available treatments for CTCL, the incremental cost-effectiveness ratio for interferon and ECP relative to methotrexate was \$21,704 and \$154,105 per successful response, respectively. The other pharmacological treatments were not cost-effective.

J-02 DEVELOPMENT AND VALIDATION OF THE FIRST MEASURE OF QUALITY OF LIFE SPECIFIC FOR PATIENTS WITH MYCOSIS FUNGOIDES/SÉZARY SYNDROME

ORAL McCaffrey S*1, Nagao M², Sepassi M², Sharma G²

¹PatientsLikeMe, Cambridge, USA; ²Actelion (US), Inc., South San Francisco, USA

INTRODUCTION: Although patient quality of life (QoL) plays a key role in the management of Mycosis Fungoides/Sézary syndrome (MF/SS), QoL is often estimated by administering generalized PROs, which are not disease-specific and may fail to capture the unique experiences of patients living with MF/SS. This presentation will review the development and psychometric evaluation of the first health-related QoL instrument specifically designed for MF/SS patients.

METHODS: Initial items for the cutaneous T-cell lymphoma (CTCL) QoL were developed through 1) a literature review, 2) interviews with key opinion leaders and CTCL patients, and 3) cognitive interviews with CTCL patients. Next, CTCL patients (N= 126) completed the 14-item CTCL QoL along with the Skindex-29. A subset (n=66) completed the CTCL QoL again 5 days later.

RESULTS: The CTCL QoL was developed using advanced Rasch measurement modelling approaches. Specifically, the Andrich-Grouped Rating Scale Model was employed, whereby items that evaluate frequency and items that evaluate intensity/severity of interference in QoL are grouped together. Two items were iteratively removed based on poor item fit, with the final model producing good item, person, and test-retest reliability. The CTCL QoL was found to be unidimensional, with 62.5% of the raw variance in interference in QoL being explained by the model. The CTCL QoL was positively correlated with the two anchors Skindex-29 and syndrome stage, providing support for convergent validity. CTCL QoL items did not evidence significant bias based on gender, age, or race. Last, Rasch scores were converted to scaled scores with qualitative descriptive categories for ease of raw score interpretation.

CONCLUSIONS: The CTCL QoL is the first disease-specific PRO instrument to measure QoL in MF/SS patients. Importantly, the patient voice was incorporated into each stage of measure development, which likely improved the relevancy and accuracy of this instrument in quantifying the patient experience. Future studies might also explore the impact of using the CTCL QoL to improve the clinical management of MF/SS.

Scientific Session J. Quality of Life & Outcomes Studies

J-03 LARGE PROSPECTIVE OBSERVATIONAL REGISTRY IN MF-CTCL

ORAL Ellen J. Kim¹, Carol Zhao², Sandy Stenger-Petersen², Peter Agron², Badri Rengarajan².

¹Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA; ²Actelion Pharmaceuticals US, Inc., South San Francisco, CA, USA.

INTRODUCTION: This registry seeks to expand the limited knowledge of clinical characteristics, disease progression, treatment and response assessment patterns, clinical status, healthcare utilization, adverse events (AEs), and quality of life (QOL) in MF-CTCL. This registry will also yield insights on real-world use of and response to mechlorethamine gel, which patients must be taking at time of enrollment. Registry design and preliminary findings will be presented.

METHODS: A multicenter, prospective observational registry of approximately 300 MF-CTCL patients receiving standard care in a real-world setting. Patients must be using mechlorethamine gel at enrollment and will be followed for 12 months (even if they discontinue mechlorethamine gel during the study). The study protocol does not mandate any procedures or specific schedule of visits except completion of QOL assessments at each clinic visit (VAS for pruritus and Skindex-29).

RESULTS: Among patients enrolled to date (n=157, with 5.5 months median duration of observation), the majority were male and stage IA/IB. At enrollment, mean age was 61 years, mean duration of MF-CTCL was 2.8 years, and mean BSA involvement was 14%. Nearly 90% of patients received \geq 1 prior MF-CTCL therapies (83% received skin-directed therapies and 34% received systemic therapies). Among recorded response assessment methods used across visits, 60% were BSA followed by mSWAT (21%), PGA (14%) and CAILS (0.3%). AEs were reported in 23% of patients, dermatitis in 9% of patients and pruritus in 5%. Less than 5% of patients experienced SAEs. Patient compliance with completing QOL assessments was approximately 85%.

CONCLUSIONS: This will be the largest prospective observational registry conducted in MF-CTCL. We expect to provide novel observations and insights into disease progression, duration of therapies, therapy combinations, therapeutic switching patterns, other clinical management patterns, and healthcare utilization. In particular, capturing QOL is a novel aspect of the study. Through stratification of patients by disease stage, BSA, disease duration, prior therapies, and other covariates, we expect to gain insights on subpopulations and improve understanding of MF-CTCL.

J-04 ASSESSMENT OF QOL, ILLNESS PERCEPTION, AND ILLNESS BEHAVIOR IN 92 PATIENTS WITH PRIMARY CUTANE-OUS LYMPHOMA

ORAL Porkert S, Lehner-Baumgartner E, Knobler R, Riedl E, Jonak C* Department of Dermatology, Medical University of Vienna, Austria

INTRODUCTION: Primary cutaneous lymphomas (CL) represent a heterogeneous group of lymphoproliferative disorders of the skin that vary widely in terms of clinical symptoms and prognosis. All patients suffering from CL experience pruritus and chronic skin alterations. These skin alterations are associated with a significant symptom burden. Until now, sparse information on psychosocial experiences of CL patients is available. Thus, we conducted a questionnaire-based study for a comprehensive data collection of Skindex-29, Illness Perception Questionnaire (IPQ-R), Scale for the Assessment of Illness Behavior (SAIB), and pruritus in CL patients. METHODS: Within this cross-sectional study, 92 patients with CTCL and CBCL were consecutively recruited at the Department of Dermatology, Medical University of Vienna, between 2014 and 2016. Data of Skindex-29, IPQ-R, SAIB, and VAS (visual analogue scale for pruritus) were evaluated in relation to clinical characteristics and sociodemographics.

RESULTS: Questionnaires of 92 CL patients were evaluated. Mycosis fungoides (MF) was present in 55 and Sézary syndrome (SS) in 2 patients. Non-MF/SS was evident in 13 patients and 15 suffered from CBCL. Advanced-stage MF/SS (n=19) was associated with higher HRQOL impairment than early-stage (n=36). Patients with advanced-stage had a high emotional burden with poor belief in treatment or personal control. Patients with non-MF/SS or CBCL were relatively unaffected by disease with no reduction in HRQOL and high perception of treatment and personal control.

CONCLUSIONS: Primary CLs are an orphan disease with great clinical variability. Our own expertise suggests a great impact of the appearance of the disease on patient's psychological burden. Further, popular web research carried out by patients often increases patients' unsureness concerning their cancer diagnosis and prognosis. Therefore, the suitable information provided by physicians on individual disease course becomes even more important. An elaborate evaluation of HRQOL, illness perception, and illness behavior in CL patients might help to improve patient care generally and elucidate patients' mental burden specifically.

J-05 CAREGIVER BURDEN AND QUALITY OF LIFE FACTORS AFFECTING CAREGIVERS OF PATIENTS WITH CUTANEOUS T-CELL LYMPHOMA

ORAL McCann S*, Astley E, Huwe J, Lipner C, Apfel A, Fabio A, Akilov O University of Pittsburgh Medical Center, Pittsburgh, PA, USA

INTRODUCTION: A unique caregiver burden and quality of life for the caregivers of CTCL patients exists, and as such, there may be unidentified, and thus unmet, caregiver needs. The purpose of this pilot study is to determine the demographics, unique caregiver burden, quality of life issues in those caring for patients with cutaneous t-cell lymphoma and the differences in caregiver burden dependent upon disease severity.

Scientific Session J. Quality of Life & Outcomes Studies

METHODS: Caregivers of patients with CTCL (mycosis fungoides/Sezary syndrome) were approached at the point of care (clinic or treatment visit) to participate in the study. The Caregiver Quality of Life-Cancer and the Burden Interview Tool were used to collect general information about the caregiver burden. In addition, the authors developed a Demographic Questionnaire to elicit more specific information about the caregiver and their experience specifically related to caring for a loved one with skin disease. Data were collected and analysed anonymously.

RESULTS: Analysis of the data will seek to demonstrate the following: 1) Caregiver demographics (age, sex, relationship to patient); 2) Caregiver perception of disease severity and known stage of patient; 3) Patient co-morbidities contributing to caregiver burden; 4) Perception of care given to caregivers by health care providers; and 5) Unique contribution of CTCL symptoms affecting QOL and caregiver burden including pruritus, scaling, physical changes, and treatments.

CONCLUSIONS: The caregiver burden experienced by carers of patients with CTCL has not been explored to the authors' knowledge. This pilot study is an important first step in identifying this unique caregiver burden and will help health care providers to recognize and address caregiver burden.

J-06 SECOND SOLID ORGAN MALIGNANCIES IN PATIENTS WITH MYCOSIS FUNGOIDES IN GREATER PITTSBURGH AREA

POSTER Mori WS*, Akilov OE

University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

INTRODUCTION: A number of retrospective studies have demonstrated an increased incidence of second malignancies among patients with mycosis fungoides (MF) or Sézary syndrome (SS). Our study goal is to measure the incidence of second malignancies among a cohort treated at University of Pittsburgh Medical Centre, providing insight on a region that to our knowledge has not been investigated before.

METHODS: The clinic-based data was obtained from the electronic health medical record using diagnosis codes for MF, SS, and any concomitant neoplasms.

RESULTS: 883 patients with MF and 196 patients with SS were identified from 1979 till 2015. Several types of cancer was found to be higher in population of MF/SS patients. Relative risk was calculated using the incidence of second malignancies in the cohort compared with an age-matched control group representing the expected number of second cancers using a cancer registry. The incidence of those findings was compared with published previously, and unique features for Greater Pittsburgh area were identified. CONCLUSIONS: This study provides valuable insight on the risk of second malignancies as well as the particular profile of second malignancies in patients with MF and SS observed among another geographic region.

J-07 COMPREHENSIVE CLINICAL DATA REVIEW OF PATIENTS SUFFERING FROM MYCOSIS FUNGOIDES WITH BAD OUT-COME

POSTER Porkert S, Venz M, Valencak J, Jonak C*

Department of Dermatology, Medical University of Vienna, Austria

INTRODUCTION: Primary cutaneous T-cell lymphomas (CTCLs) comprise heterogeneous entities of extra nodal non-Hodgkin lymphomas, deriving from skin-homing or resident T-cells. Mycosis fungoides (MF) displays its most common subtype. Within MF, a large variety from a clinical indolent course up to lethal outcome exists. However, knowledge of specific markers for prediction of prognosis is still sparse. To date, only few studies aiming to elucidate predictive parameters in CTCL were performed. Thus, we processed clinical data of 24 MF patients with disease-related death.

METHODS: In this retrospective study, all included patients were diagnosed and treated at the Department of Dermatology, Medical University of Vienna, between 2000 and 2015. Clinical course and histopathological findings were compared within this group and with existing literature.

RESULTS: The majority of patients were male (66.7%) with an average age of 60.9 years at diagnosis. An average time of 2.7 years between onset of specific symptoms and confirmed diagnosis was recorded. At time of diagnosis, 58.3% presented with advanced-stage disease. Advanced-stage was associated with average survival of 5.9 years and early-stage with 9.8 years. Advanced-stage disease shortened life by about 2.7 years. Large-cell transformation (LCT) and folliculotropism (FT) were found in 54.2% and 16.7% of patients, respectively. Serum LDH levels ranged between 131 U/I and 440 U/I. Secondary malignancies were observed in 25% of this collective.

CONCLUSIONS: Although results were not expected to be reliable due to small numbers, we could confirm specific parameters for MF as follows: gender distribution, average age, average time to diagnosis, rate of FT, worse outcome of LCT, and association with secondary malignancies. Despite paramount advances in cancer research and therapy were achieved in recent years, MF is still incurable. In this orphan disease, there is a high need for prospective randomized clinical trials and fundamental studies, which may hopefully lead to improved conception of this often debilitating disease.

Scientific Session J. Quality of Life & Outcomes Studies

J-08 SKIN INFECTION IN MYCOSIS FUNGOIDES AND SÉZARY SYNDROME

POSTER Yoo J¹*, Shah F¹, Lewis H¹, Martin-Clavijo A¹, Stevens A², Chaganti S³, Scarisbrick JJ¹ ¹Department Dermatology, ²Oncology, ³Haematology, ⁴Oncology, University Hospital Birmingham, Birmingham UK

INTRODUCTION: Mycosis fungoides (MF) and Sézary syndrome (SS) have a high rate of infection contributing to >50% of deaths with skin being the most common site probably due to skin barrier defect and reduced T-cell immunity. Other common T-cell mediated dermatoses, such as eczema (T helper2-mediated(Th2)) and psoriasis (Th1-mediated), are also susceptible to skin infection but direct comparison amongst these skin conditions has not been studied.

METHODS: We compared infection rates amongst MF/SS (n=139), eczema (n=188) and psoriasis (n=385) patients attending our Dermatology outpatient clinic (1/6/2015-1/6/2016). In MF/SS patients, we also compared stage, age and blood parameters (lymphocyte, CD4:CD8 counts) in those with/without infections.

RESULTS: Among 712 patients, skin infection was most common in MF/SS (27/139, 19.4%) followed by eczema (29/188, 15.4%) and psoriasis (18/385, 4.7%). The skin infection rates in MF/SS increased significantly with overall stage from 9% in stage I to 56% in stage IV (p<0.001) as well as with TNB class; T1=3%vs.T4=33% (p=0.003), N0=13%vs.N3=50% (p=0.002) and B0=16%vs.B2=57% (p=0.002). There was no difference in age or CD4:CD8 counts. Stage progression in MF has been associated with a change from Th1 to Th2-mediated dominance. Considering this, there was significant increase in skin infection in Th2-mediated diseases, eczema and advanced MF/SS (46/243, 18.9%), compared to Th1-mediated diseases, psoriasis and early MF (28/468, 6%) (p<0.001).

Staphylococcus aureus was the commonest organism; MF/SS (31/47,66%), eczema (42/56;75%) and psoriasis (16/25;72%). Methicillin-resistant Staphylococcus aureus was more frequently observed in MF/SS (9/47;19.1%) than eczema (8/56;14.3%) or psoriasis (1/25;4%) (p=0.212). In MF/SS, other species included Candida (3/47;6.4%), Streptococcus (2/47;4.2%), Herpes (1/47;2.1%) and Serratia (1/47;2.1%).

CONCLUSIONS: This study demonstrated significantly increased skin infection rate with advancing stage of MF/SS. Similarly high rates of infection were seen in eczema and we report that skin diseases with Th2-predominance, have a significantly higher skin infection rate compared to Th1-driven diseases (p<0.001). *Staphylococcus aureus* has been implicated as a driver in atopic eczema because of its ability to produce superantigens and this may also be important in progression of MF to SS with the switch from a Th1 to Th2 mediated drive.

J-09 PROGNOSTIC FACTORS IN ELDERLY PATIENTS WITH MYCOSIS FUNGOIDES AND SEZARY SYNDROME

POSTER Kheterpal M*¹, Lebowitz E², Flores E¹, Pulitzer M¹, Horwitz S¹, Moskowitz A¹, Myskowski PL¹ ¹Memorial Sloan Kettering Cancer Center, New York, NY, USA. ²Weill Cornell Medical College, New York, NY, USA

INTRODUCTION: Older age is an independent poor prognostic sign in mycosis fungoides (MF) and Sezary syndrome (SS) patients, although few characteristics are known to explain this observation. Our objective was to identify unique factors predicting poor outcomes in this population.

METHODS: Staging data for 174 patients with MF/SS diagnosed at the age of 65 or older was included in disease specific survival (DSS) and progression of disease (POD) analysis. Eleven historical and clinical factors were recorded at presentation: age, gender, co-morbidities (including hypertension, hyperlipidemia, diabetes, heart disease and history of other malignancies), history of immunosuppression (prior history of immunosuppressive medications n=11, history of prior chemotherapy n=9, history of CLL n=8), presence of lymphomatoid papulosis (LyP), family history of lymphoma, plaques involving >10% body surface area (BSA) in early stage patients, folliculotropic MF, clinical and T-staging and elevated LDH. Each factor was tested against POD (defined as change in clinical stage or death from MF) and DSS.

RESULTS: Median age at presentation in this study was 72 (range, 65-101) years with a mean follow up of 4.5 years (range, 1.1-22.1). Most patients (75.3%) presented in early stages (Stage IA-IIA), however, 21 (12%) patients presented with stage IV disease, with 47.6% (n=10) with less than 1 year history of any skin lesions. In a multivariate analysis, DSS was worse with increasing age ($p \le 0.05$), history of immunosuppression (p < 0.01), family history of lymphoma (p < 0.01), plaque burden >10% BSA in early stage (p < 0.05), elevated LDH (p < 0.01), advanced clinical stage (p < 0.01) and T stage (p < 0.01). POD was significantly higher in patients with history of immunosuppression, family history of lymphoma, extensive plaque burden, elevated LDH, as well as advanced clinical and T-stages. POD was not found to be significant with presence of folliculotropic MF, 3 or more medical comorbidities or concomitant LyP. CONCLUSIONS: Elderly MF/SS patients may have a more aggressive course due to higher incidence of advanced clinical stage at presentation than expected (based on literature data for all-ages). Unique factors predictive of an aggressive phenotype were prior immunosuppression, plaque burden in early stage disease, and family history of lymphoma. Comparison with cohort of elderly MF/SS patients diagnosed at a younger age is warranted.

* indicates presenting author

Scientific Session K. Clinical Aspects

K-01 CUTANEOUS LYMPHOMAS DURING ANTI-TUMOR NECROSIS FACTOR THERAPY ARE OFTEN ASSOCIATED WITH MISDIAGNOSED "PSORIASIS" OR POORLY CHARACTERIZED "DERMATITIS"

ORAL Martinez-Escala ME*1, Sable KA1, Posligua AL1, Pro B2, Kaplan J2, Choi J1, Guitart J1

¹Departments of Dermatology, Northwestern University, Feinberg School of Medicine. Chicago, IL; ²Department of Medicine, Division of Hematology/Oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Feinberg School of Medicine. Chicago, IL

INTRODUCTION: Several cases of cutaneous lymphoma (CL) have been reported in patients receiving anti-tumor necrosis factor α (anti-TNF) therapy. Whether anti-TNF causes or unmasks previously undiagnosed CL is a matter of debate. The goal of this project was to characterize our experience with CL in the setting of anti-TNF therapy.

METHODS: A retrospective 10-year database review was conducted to identify cases of cutaneous T-cell (CTCL) or B-cell lymphoma (CBCL) that were diagnosed after treatment with anti-TNF therapy.

RESULTS: Sixteen cases were identified, including 14 CTCL and 2 CBCL. The cohort included 12 male and 5 female with a median age of 64 years (21-76). Anti-TNF was prescribed mostly for presumed psoriasis or unspecified dermatitis (n=11), as well as rheumatoid arthritis (RA) (n=3) and inflammatory bowel disease (IBD) (n=2). One RA patient and one IBD patient reported an unspecified dermatitis previous to anti-TNF therapy. Median time since anti-TNF therapy initiation until CL diagnosis was 8 months (1–51). Ten patients received at least one systemic immunesupressant before anti-TNF therapy. CTCL cases included 10 mycosis fungoides, 1 Sézary syndrome, 3 cytotoxic CTCL. Skin involvement tended to be extensive (2T1, 2T2, 6 T3, 4 T4) with nodal involvement in 5 patients and peripheral blood involvement in 4 patients (3 with B1 and 1 B2). Upon follow-up, 5 patients were alive without disease (2 following allogenic stem cell transplant), 5 had PR to various treatment, 2 patients had disease progression, one patient dead of disease, and 2 lost to follow-up. The CBCLs involved the skin only and included 1 marginal zone lymphoma and 1 follicle center lymphoma. Both patients are alive without disease.

CONCLUSIONS: We conclude that most CL associated with anti-TNF therapy had a preceding skin conditions (13/16) probably misdiagnosed as "psoriasis" or unspecified dermatitis. The advanced stage at diagnosis suggests that anti-TNF therapy may unmask previously undiagnosed CL and accelerate disease progression. There is a need to raise awareness of these events in the medical community as well as recommend morphological and molecular evaluation of skin and peripheral blood analysis in patients with atypical presentations of "psoriasis" or undiagnosed dermatitis prior to initiation of anti-TNF therapy.

K-02 POOR OUTCOME OF PATIENTS WITH TRANSFORMED MYCOSIS FUNGOIDES: ANALYSIS FROM A PROSPECTIVE MULTICENTER US COHORT STUDY

ORAL Lansigan F¹*, Horwitz SM², Pinter-Brown LC³, Carson KR⁴, Shustov AR⁵, Rosen ST⁶, Pro B⁷, His ED⁸, Federico M⁹, Gisselbrecht C¹⁰, Schwartz M¹¹, Bellm LA¹¹, Acosta M¹², Foss FM¹³

¹Dartmouth Hitchcock Medical Center, Hanover, NH, USA; ²Memorial Sloan-Kettering Cancer Center, New York, NY, USA; ³University of California, Irvine, Irvine, CA, USA; ⁴Washington University School of Medicine, St Louis, MO, USA; ⁵Fred Hutchinson Cancer Research Center, Seattle, WA, USA; ⁶City of Hope Medical Center, Duarte, CA, USA; ⁷Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL, USA; ⁸Cleveland Clinic, Cleveland, OH, USA; ⁹University of Modena and Reggio Emilia, Modena, Italy; ¹⁰Hôpital Saint Louis, Paris, France; ¹¹MedNet Solutions, Minnetonka, MN, USA; ¹²Spectrum Pharmaceuticals, Inc., Irvine, CA, USA; ¹³Yale University, New Haven, CT, USA

INTRODUCTION: We examined patient characteristics, treatments and outcomes of transformed mycosis fungoides (T-MF) patients from COMPLETE: a large, multicenter, prospective cohort study of peripheral T-cell lymphoma patients in the US.

METHODS: Patients with T-MF were enrolled in COMPLETE at the time of transformation. For this analysis, we identified T-MF patients with completed baseline, treatment and follow-up records. Median survival was assessed using Kaplan-Meier methodology. RESULTS: Of the 499 patients enrolled in COMPLETE, 17 had T-MF. Table 1 summarizes patient and treatment characteristics at transformation. Median age was 61; 53% were male, 9 had elevated lactate dehydrogenase (LDH) and 9 had lymph node involvement. About one-quarter of the patients were black and 47% had CD30+ disease. Median time to transformation was 53 months. All patients received systemic therapy, with 19% receiving concomitant radiotherapy. Most patients (87%) received single agents, including liposomal doxorubicin, pralatrexate and gemcitabine. Eight patients (50%) had reported responses to therapy. Median survival was 18 months (Figure 1). One- and two-year survival rates were 56% and 44%, respectively.

CONCLUSIONS: T-MF often express CD30 and present with lymph-node involvement. Responses have been seen with single agents but survival remains poor. Novel treatment approaches are urgently needed to improve outcomes.

Scientific Session K. Clinical Aspects

Patient Characteristics at Transformation	N = 17	
Median age (range), years Median time to transformation (range), months	61 (57-71) 53 (49-74)	
Male Sex	9 (53%)	
Race White Black	13 (76%) 4 (24%)	
Elevated LDH	9 (53%)	
CD30 expression Positive Negative Not assessed	8 (47%) 7 (41%) 2 (12%)	
Lymph node involvement	9 (53%)	
Visceral disease	1 (6%)	
First Treatment after Transformation	N = 16	
Treatment approach Local radiotherapy + chemotherapy Chemotherapy	3 (19%) 13 (81%)	
Systemic therapies* Liposomal doxorubicin Pralatrexate Gemcitabine CHOP/CHOP-like + etoposide Alisertib Dexamethasone Vorinostat	5 (33%) 3 (20%) 2 (13%) 2 (13%) 1 (7%) 1 (7%) 1 (7%)	
Best response Complete response Partial response Stable disease Progressive disease	2 (13%) 6 (38%) 1 (6%) 7 (44%)	



*Therapy is missing for one patient.

Table 1.

K-03 SÉZARY SYNDROME WITHOUT ERYTHRODERMA

ORAL Maubec E¹, Henn A², Michel L³, Fite C², Deschamps⁴ L, Ortonne N⁵, Ingen-Housz-Oro S⁶, Marinho E⁴, Beylot-Barry M⁷, Bagot M⁸, Laroche L¹, Crickx B², Laroche L¹*

¹Assistance Publique des Hôpitaux de Paris (APHP), Hôpital Avicenne, Dermatology Department, University of Paris 13, Bobigny, France. ²APHP, Hôpital Bichat-Claude-Bernard, Dermatology Department, Université Paris 7-Denis Diderot, PRES Sorbonne-Paris Cité, Paris, France. ³Institut National de la Santé et de la Recherche Médicale (INSERM) U976, Hôpital Saint-Louis, Paris, France. ⁴APHP, Hôpital Bichat-Claude-Bernard, Pathology Department, Paris, France. ⁵APHP, Groupe Hospitalier Henri-Mondor, Pathology Department, Créteil, France; Université Paris Est-Créteil, Créteil, France. ⁶APHP, Groupe Hospitalier Henri-Mondor, Dermatology Department, Créteil, France: ⁷Centre Hospitalo-Universitaire (CHU) de Bordeaux, Dermatology Department, Université de Bordeaux, Bordeaux, France; EA2406, Université de Bordeaux, Bordeaux, France. ⁸Université Paris 7-Denis Diderot, PRES Sorbonne-Paris Cité, Paris, France; APHP, Hôpital Saint-Louis, Dermatology Department, Paris, France.

INTRODUCTION: Sézary syndrome is a cutaneous T-cell lymphoma characterized by erythroderma and leukemic involvement. We sought to define the clinical, biologic and histopathologic features of Sézary syndrome without erythroderma.

METHODS: Features of patients with Sézary syndrome and normal-appearing skin or stage-T1 patches, fulfilling Sézary syndrome hematologic criteria and with histologically documented disease in normal-appearing skin were collected. Expression of Sézary syndrome molecular biomarkers in peripheral blood and skin lymphocytes were studied.

RESULTS: Five women and 1 man (median age: 71 years) were all referred for generalized pruritus. Four had no specific lesions; 2 had T1-stage patches. Histologic examination of normal-appearing skin from all patients showed lesions compatible with Sézary syndrome. Peripheral blood lymphocytes from 3 of 4 patients tested strongly expressed PLS3, Twist-1, and KIR3DL2. All normal-appearing skin biopsy specimens expressed programmed death-1. Median follow-up was 9 years. Although no patient developed erythroderma, tumors, or abnormal lymph nodes, specific skin lesions appeared in all patients during follow-up. Only 1 death, unrelated to Sézary syndrome, occurred.

CONCLUSIONS: Sézary syndrome without erythroderma is a rare entity that may have a better prognosis than classic Sézary syndrome. In clinical practice, in a case of unexplained chronic pruritus without cutaneous signs, a complete blood cell count with Sézary cell count and a skin biopsy specimen of normal-appearing skin for histology, immunophenotyping, and T-cell receptor gene rearrangement studies should be performed. The study of this entity could help to decipher mechanisms of erythroderma and develop new insights into prognosis of Sézary syndrome.

Scientific Session K. Clinical Aspects

K-04 RISK OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH PARAPSORIASIS (EARLY MYCOSIS FUNGOIDES): A DANISH NATIONWIDE POPULATION-BASED COHORT STUDY

ORAL Lindahl LM¹*, Schmidt M², Farkas DK², Sørensen HT², Iversen L¹

¹Department of Dermatology, Aarhus University Hospital, Denmark and ²Department of Clinical Epidemiology, Aarhus University Hospital, Denmark

INTRODUCTION: Parapsoriasis can be considered an early stage of mycosis fungoides (MF). It is an indolent type of cancer in a chronic inflammatory environment. As active cancers and inflammation profoundly impact the risk of venous thromboembolism (VTE), we examined the risk of VTE in patients with parapsoriasis.

METHODS: Using the Danish nationwide population-based registries, we identified 634 patients with parapsoriasis, who were treated at a hospital department of dermatology (where histological verification of the diagnosis was standard) and followed for up to 19 years. Using proportional hazards regression as a measure of relative risk (RR), we assessed the association between first-time VTE event in patients with parapsoriasis compared with a randomly selected sex- and age-matched comparison cohort from the general Danish population. The VTE events were subdivided into provoked VTE, defined by VTE associated with classical risk factors, and unprovoked VTE occurring in absence of classical risk factors for VTE.

RESULTS: The absolute risk (cumulative incidence) of unprovoked VTE for patients with parapsoriasis 5 and 10 years after diagnosis was 0.9% (95% confidence interval (CI) 0.3%-2.0%) and 1.7% (95% CI 0.8%-3.3%), respectively. Notably, the absolute risk was lower for the population comparison cohort after 5 and 10 years, 0.4% (95% CI 0.3%-0.6%) and 1.0% (95% CI 0.7%-1.3%), respectively. These differences yielded a 2.7-fold increased RR of unprovoked VTE in patients with parapsoriasis compared with the general population (2.67, 95% CI 1.32-5.40). Interestingly, according to stratification by follow-up time, the RR of unprovoked VTE was driven by the risk increase after more than 5 years of follow-up, RR 3.96 (95% CI 1.43-10.95).

CONCLUSIONS: Patients with parapsoriasis had a 2.7-fold increased risk of unprovoked VTE. The risk increased with time since diagnosis, indicating that long-term malignant proliferation and inflammation impacts venous hemostasis and coagulability as the underlying cause of VTE. These new findings may have implications for clinical handling and monitoring of early MF in the future.

K-05 PROTEAN MANIFESTATIONS OF EARLY SÉZARY SYNDROME

ORAL Thompson A¹, Davis MD¹, Mangold AR², Cozzio A³, Guenova-Hotzenecker E, Hodak E⁴, Pujol R⁵, Pittelkow MR², Gniadecki $R^{*6,7}$

¹Mayo Clinic, Rochester, Minnesota, USA; ²Mayo Clinic, Scottsdale, Arizona, USA; ³Dept Dermatology, University Hospital Zurich, Switzerland; ⁴Department of Dermatology, Rabin Medical Center, Petah Tikva, University of TelAviv, Israel; ⁵ Department of Dermatology, Hospital del Mar, Universitat Autònoma de Barcelona, Spain; ⁶University of Alberta, Edmonton, Alberta, CA; ⁷ Department of Dermatology, University of Copenhagen, Denmark;

INTRODUCTION: Sézary syndrome (SS) is a leukaemia-lymphoma syndrome involving the skin, blood and the lymph nodes. Classic, SS is defined by erythroderma, generalized lymphadenopathy, and the presence of circulating malignant T cells in peripheral blood. However, many patients present with non-erythrodermic SS. The aim of this study is to clarify the clinical characteristics of patients with SS.

METHODS: A retrospective, multicentre chart review of 264 (Barcelona – n=11 cases (2003-2015), Copenhagen n=18 (2002-2014), Mayo Clinic n=192 (1973-2009), Tel-Aviv n=18 (1996-2015), Zurich n=25 (2000-2015) confirmed cases of SS was performed. The diagnosis of SS was defined by: presence of erythroderma, lymphadenopathy, skin biopsy compatible with cutaneous T-cell lymphoma (CTCL), blood involvement (Sézary cell count >1000/ul and/or CD4/CD8>10 by flow cytometry), presence of monoclonal TCR population in peripheral blood and bone marrow involvement.

RESULTS: At time of diagnosis, only 6 patients met all diagnostic criteria of SS; 40.2% - 4 criteria, 28.8% - 3 criteria, 18.2% - 5 criteria, 10.8% - 2 criteria. In most patients (n=228), erythroderma was present at diagnosis. 34 patients (12.9%) were non-erythrodermic at the initial presentation. 19/34 (56%) non-erythrodermic patients progressed to erythroderma. The non-erythrodermic phenotype included: atopic dermatitis-like rash (8.8%), dermatitis (2.9%) or patches and plaques of mycosis fungoides (26.5%). 20/34 (58.8%) presented with minimal skin disease. There was no difference in mean age, sex, or overall survival difference between erythrodermic and non-erythrodermic presentation of SS. Of the patients with a dermatitis-like presentation, they tended to be younger and had a longer survival than those with erythrodermic SS. There was a significant diagnostic delay in non-erythrodermic SS patients.

CONCLUSIONS: We report the largest cohort of patients with SS to date. The clinical presentation of SS can vary widely. Erythroderma SS is the most common presentation; however, it may develop late in SS. Non-erythrodermic SS may have an early, indolent phase which delays diagnosis. Early skin signs in SS fall into the following 5 distinct categories: 1) typical erythroderma with or without blood involvement, 2) prolonged (>1 year) dermatitis without erythroderma, 3) atopic dermatitis-like, 4) patches and plaques of mycosis fungoides, 5) primary leukaemia.

Scientific Session K. Clinical Aspects

K-06 CUTANEOUS ANAPLASTIC LARGE CELL LYMPHOMA: A COMPARATIVE CLINICAL FEATURE AND SURVIVAL OUT-COME ANALYSIS OF 52 CASES ACCORDING TO PRIMARY TUMOR SITE

POSTER Jin Lee WJ*, Moon IJ, Lee MW

Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

INTRODUCTION: Cutaneous anaplastic large cell lymphoma is primary extranodal or secondary to nodal disease. We analysed clinical features and survival outcomes by primary tumor site in patients with cutaneous anaplastic large cell lymphoma (LCL). METHODS: Clinical features, survival outcomes and prognostic factors of 52 patients with primary or secondary cutaneous ALCL to primary nodal disease were retrospectively evaluated using medical records.

RESULTS: Although skin lesion characteristics did not significantly differ between groups, the head and neck location was more common in primary cutaneous ALCL, whereas cutaneous lesion extent was greater in secondary cutaneous ALCL. Skin lesion extent in primary cutaneous ALCL was indicative of extracutaneous dissemination development and skin lesion relapse. Neither anaplastic lymphoma kinase expression nor clinical stage affected skin lesion characteristics in secondary cutaneous ALCL. Patients with primary rather than secondary cutaneous ALCL demonstrated better survival outcomes. The skin lesion extent and location on the leg were associated with the tendency toward a poorer prognosis in primary cutaneous ALCL. The secondary cutaneous ALCL prognosis was not influenced by skin lesion characteristics.

CONCLUSIONS: Survival outcomes and prognostic factors in cutaneous ALCL differed by primary tumor site.

K-07 SUBCUTANEOUS PANNICULITIS LIKE T-CELL LYMPHOMA: 15 YEAR EXPERIENCE OF THE GREATER MANCHESTER SUPRA-REGIONAL CUTANEOUS LYMPHOMA MULTI-DISCIPLINARY TEAM.

POSTER Parry E^{*1}, Jamieson L², Motta L², Green R², Menasce L³, Shenjere P³, Smith E³, Bloor A³, Illidge T³, Cowan R³ ¹Tameside Hospital NHS Foundation Trust, ² Salford Royal Foundation Trust, ³ The Christie Hospital Foundation Trust, Manchester, UK.

INTRODUCTION: Subcutaneous panniculitis like T-cell lymphoma (SPLTCL) is a rare subtype of CTCL. We present the 15-year experience of our multi-disciplinary team (MDT).

METHODS: Retrospective case note review of 13 patients referred to MDT with suspected SPLTCL summarizing clinical, histological, treatment and response data.

RESULTS: Clinicopathological correlation diagnosed 8 with SPLTCL: M=F; age 18-89 years; symptom duration 2 months to 6 years; 7 had multifocal lesions, limbs commonest site; 50% had systemic symptoms. Histology findings: atypical lymphocytic infiltration in sub-cutis; rimming of adipocytes; fat necrosis; CD3+/CD8+/BF-1+/TIA+ /CD 4-/CD56- phenotype. Staging investigations: enlarged regional lymph nodes in 2; 1 involved by SPLTCL on biopsy; pancytopenia in 2; 1 mild haemophagocytic syndrome on bone marrow biopsy. Management depended on symptoms and co-morbidities: 2 elderly males died within 12 months of diagnosis; 1 received palliative care; 1 oral Prednisolone and local radiotherapy. 4 patients < 21 years at diagnosis are in CR: 1 underwent spontaneous remission; 2 oral Prednisolone 0.5 mg/Kg tapered over 2-12 months; 1 with stage IVA disease received chemotherapy for resistant disease after oral steroids: both had Gemcitabine with PD, 1 then achieved CR after CHOP and auto-SCT; 1 achieved PR with Bexarotene and local radiotherapy. Overall 5 (62.5%) remain in CR with RFS 6 months – 12 years. Clinicopathological correlation diagnosed 5 with benign disease: 3 F; age 18-43 years; 3 lupus panniculitis; 1 possible lupus panniculitis/SPLTCL overlap underwent spontaneous remission; 1 cytotoxic lymphomatoid papulosis.

CONCLUSIONS: Our experience confirms SPLTCL is a rare disease with heterogeneous clinical presentation and treatment response. Oral steroids were commonest initial therapy. Overall survival in our cohort was 75%.

K-08 AN EVIDENCE BASED APPROACH TO REFRACTORY SEZARY SYNDROME

POSTER Ahmad A*, Doll DC

University of Missouri, Columbia, Missouri

INTRODUCTION: Sezary Syndrome is an aggressive and rare subtype of cutaneous T cell lymphoma. There is no standard therapy for initial or relapsed disease and experts differ in their preferred approach. We present to you a case of Sezary syndrome that was refractory to multiple lines of therapy. We then review the literature regarding initial and subsequent therapies.

METHODS: We present a case of aggressive Sezary Syndrome that was refractory to multiple lines of therapy. We then describe a Pub Med literature search that was conducted to elucidate the best initial and subsequent therapy for Sezary Syndrome. We describe the strengths and perils of various modalities of treatment. We attempt to grade the evidence to help formulate what we believe constitutes the best first line therapy and subsequent therapy.

RESULTS: 1) The initial treatment approach to Sezary Syndrome without visceral disease consists of systemic therapy. Options include, extracorporeal photopheresis (ECP), retinoids, interferons, histone deacetylase inhibitors, or low dose methotrexate. These agents can be combined together or provided in conjunction with skin directed therapies (topicals, phototherapy, TSEBT, etc.). Our literature review suggests combining ECP with biological modifiers leads to the quickest and best response rates. 2) The initial treatment approach to Sezary Syndrome with visceral disease consists of systemic therapy utilizing either histone deacetylase inhibitors or systemic chemotherapy. The patient in our vignette was treated initially with single agent pegylated liposomal doxorubicin. Our

Scientific Session K. Clinical Aspects

literature review suggested an overall response rate between 40-90% when this agent is used as first therapy. 3) Relapsed disease occurs in the majority of patients and these patients should be encouraged to participate in clinical trials. Outside of clinical trials choices include, skin-directed therapy or systemic therapy. The patient in our vignette, after progressing on liposomal doxorubicin, was treated with romidepsin. Our literature review suggested an overall response rate of 34% when this agent is used in the refractory setting. The patient progressed and was subsequently treated with bexarotene and ECP. After relapse patient was treated with mogamulizumab. Our literature review supports around a 37% overall response in the refractory setting. However, this patient did not respond. Finally, patient was treated with alemtuzumab. Our literature review suggests an overall response rate between 86-100% when this agent is used in the relapsed setting. Patient has been in complete remission for a year.

CONCLUSIONS: 1) The initial approach to Sezary Syndrome with or without visceral disease is controversial with no clearly defined first line therapy. Our literature review suggests that without visceral disease, the ideal first line therapy should be ECP combined with a biological modifier. This leads to a robust overall response and is associated with the least amount of adverse side effects. With visceral disease, the literature does not suggest a clear first line modality. We advocate the use of either single agent chemotherapy or a histone deacetylase inhibitor. 2) There are a host of mediations that have efficacy in the relapsed setting. Again, no clear standard of care exists. We advocate clinical trials for these patients. Outside of a clinical trial, our literature review suggests efficacy for various systemic therapies as well as skin-directed therapies. Our patient ultimately had an excellent response to alemtuzumab. Indeed, our literature review found several studies where the overall response rate was noted to be between 86-100%.

K-09 CLINICAL SERVICE EVALUATION OF THE NEW IPAD SKIN WEIGHTED ASSESSMENT TOOL (ISWAT)FOR PATIENTS WITH MYCOSIS FUNGOIDES.

POSTER Kuciejewska A*, Kiely C, Salam A, Urwin R, Mcormick G, Whittaker S, Child F, Wain M, Morris SL St Johns Institute of Dermatology, Guys Hospital, Graze Maze Pond , London SE1 9RT

INTRODUCTION: Management of Mycosis Fungoides requires regular assessment of the severity of skin involvement. The modified severity-weighted assessment tool (mSWAT) was incorporated into an iPhone app in 2012. The success of the iPhone app led to the development of an iPad version.

METHODS: The aim of the iPad application was to improve the ease and accuracy of the assessment using new technology. It allows the user to paint on the screen body map the extent of the lesions differentiating for lesion types. The application then calculates the mSWAT score using a grid-point counting method and provides an image to be saved for future reference. To differentiate between the two applications we refer to this score as the iSWAT. A prospective service evaluation study of the iSWAT in 50 patients has been set up. The aim is to compare to the scores for mSWAT (using the iPhone application) and iSWAT (using the iPad application) on individual patents. We aim to asses 50 patients. The assessment is performed by two different clinicians. Each patient therefore is assessed 4 times. By comparing the scores we will determine the reproducibility between the two applications. We will also assess time efficiency, inter-observer reliability and collect the feedback from the clinicians, detailing their experience and preference for either application.

RESULTS: We have collected data on 10 patients so far. Initial results show a positive correlation between the mSWAT and iSWAT, r=0.9819, n=20, p<0.0001. The median time taken for the mSWAT was 3 minutes, and for the iSWAT was 2.3 minutes. The clinician feedback has been very positive.

CONCLUSIONS: Initial results show the Ipad iSWAT assessment may improve the ease and accuracy of skin assessment for patient with Mycosis Fungoides.

* indicates presenting author

Abstracts

Scientific Session L. Applied Research

L-01 AN IN VITRO MODEL OF PSORALEN ULTRAVIOLET A (PUVA)-INDUCED APOPTOSIS OF CUTANEOUS LYMPHOMA CELL LINES: AUGMENTATION BY TYPE I INTERFERONS VIA JAK1-STAT1 PATHWAY

ORAL Liszewski W¹, Naym DG¹, Biskup E¹, Gniadecki R^{1,2,3}

¹Department of Dermatology, Bispebjerg Hospital, Bispebjerg Bakke 23, Copenhagen, Denmark; ²Faculty of Health Sciences, University of Copenhagen, Denmark; ³Division of Dermatology, University of Alberta, Edmonton, Canada

INTRODUCTION: Photochemotherapy with psoralen and ultraviolet A (PUVA), with or without adjuvant interferon- α (IFN- α), are first line therapies for early stage mycosis fungoides and other forms of cutaneous T-cell lymphoma (CTCL). However, the mechanism by which PUVA with IFN- α work in CTCL is poorly understood. The aim of this study was to develop an in vitro model which enables to investigate the mechanisms of PUVA and PUVA with IFN- α in CTCL cells.

METHODS: An in vitro model to study the molecular mechanisms of PUVA was created using two different CTCL cell lines, MyLa, which has functional p53, and HuT-78, in which p53 is inactivated due to a homozygous nonsense mutation.

RESULTS: PUVA caused G2/M cell cycle block and apoptosis of MyLa and HuT-78 accompanied by increase in the expression of the mitochondrial proapoptotic genes Bax and PUMA and a downregulation in antiapoptotic Bcl-2. IFN-α augmented PUVA-induced apoptosis in vitro. P53 was induced and c-Myc was repressed by PUVA, but were not essential for PUVA-induced apoptosis. The adjuvant effect of IFN-α occurred via JAK1 pathway and could be inhibited by ruxolitinib.

CONCLUSIONS: PUVA induces the p53-independent aopotosis is CTCL cell lines and this process is augmented by type I interferons via JAK1 pathway.

L-02 MYD88 MUTATIONS IN A DISTINCT TYPE OF CUTANEOUS MARGINAL ZONE LYMPHOMA WITH A NON-CLASS SWITCHED IGM-IMMUNOPHENOTYPE

ORAL Wobser $M^{*1#}$, Maurus $K^{2#}$, Roth S², Appenzeller S³, Weyandt G¹, Goebeler M¹, Rosenwald A², Geissinger E² # both authors contributed equally.

¹Department of Dermatology, University Hospital Wuerzburg, Germany; ²Institute of Pathology, Comprehensive Cancer Center, University of Wuerzburg, Germany; ³Core Unit Bioinformatics, Comprehensive Cancer Center, University Hospital Wuerzburg, Germany

INTRODUCTION: Druggable somatic mutations in the MYD88 gene, leading to constitutive oncogenic NFkB- and JAK-mediated downstream signaling, underlie the molecular pathogenesis of different subtypes of Non-Hodgkin B-cell lymphomas. While prognostically relevant genomic alterations of MYD88 are also present in primary cutaneous diffuse large B-cell lymphoma, such molecular aberrations have up to now not been identified in other subtypes of indolent cutaneous B-cell lymphomas including primary cutaneous marginal zone lymphoma (PCMZL).

METHODS: Among a series of 8 PCMZL we performed in a first step panel sequencing of selected oncogenic genes involved in B-cell lymphomagenesis enriched with a HaloPlexHS-kit using the MiSeq-platform. In a next step, analyses were extended to a larger cohort of PCMZL (51 cases in total) by Sanger sequencing.

RESULTS: Among a series of 51 PCMZL we encountered 3 cases (5.9 %) harboring activating somatic MYD88 mutations (recurrent MYD88 NM_002468.4:c.794T>C, p.L265P in 2 cases, MYD88 NM_002468.4:c.695T>C, p.M232T in 1 case). Of note, all of these 3 cases with MYD88-mutated PCMZL showed tissue expression of the IgM heavy chain (3 out of 6 IgM-positive cases (50 %)), while the remaining non-IgM-restricted cases were negative for respective oncogenic MYD88 mutations.

CONCLUSIONS: By identifying a pivotal oncogenic mutation in a subset of PCMZL we have made a first step towards elucidation of the mutational landscape of PCMZL.

L-03 ANALYSIS OF THE EXPRESSION AND ACTIVITY OF METALLOPROTEINASES 2 AND 9 AND THEIR INHIBITORS AND CORRELATION WITH HISTOLOGICAL FINDINGS AND PROGNOSIS IN MYCOSIS FUNGOIDES.

ORAL Vasconcelos R*, Fanelli C, Sakai-Valente NY, Cury-Martins J, Miyashiro DR, Sanches JA University of Sao Paulo Medical School, São Paulo, Brazil

INTRODUCTION: Metalloproteinases are known by the degradation of extracellular matrix and other stages of oncogenesis, such as angiogenesis and metastatic niche formation. The gelatinases (MMP2 and MMP9) and their tissue inhibitors (TIMP1 and TIMP2, respectively) have been studied in non-Hodgkin's lymphoma nodal and correlated with prognosis. There are few studies on gelatinases and none of TIMP in cutaneous lymphomas. The objective of the study is To study the expression and activity of MMP2 and MMP9 and the expression of TIMP2 and TIMP1 in mycosis fungoides and correlate the findings with histological findings and prognosis.

METHODS: Skin biopsies of 53 cases of MF (10 MF patch, 24 poikilodermatous MF, 9 non-transformed tumor MF and 10 transformed tumor MF) were stained by immunohistochemistry for MMP2, TIMP2, MMP9 and TIMP1. The activity of MMP2 and MMP9 was evaluated by gelatin zymography.

RESULTS: MMP2 was more expressed in the epidermis and superficial dermis in patch MF cases and poikilodermatous MF (pMF),

Scientific Session L. Applied Research

compared to tumor MF (tMF). The MMP2 activity was higher in the transformed tMF. TIMP2 was significantly expressed in the epidermis of tMF than in the other groups. In the deep dermis, there was increased expression of TIMP2 in tMF. MMP9 was more expressed in the epidermis and superficial dermis in patch MF compared to the pMF. There was also high expression of MMP9 in the epidermis of MFT. In the deep dermis, the MMP9 expression was increased in the pMF, patch MF and tMF. The MMP9 activity by zymography was higher in non-transformed tMF. TIMP1 was more expressed in patch MF compared to pMF in the epidermis, superficial and deep dermis.

CONCLUSIONS: MMP2 and MMP9 were markers of activity for MF. TIMP-1 was expressed similarly to MMP9. TIMP-2, in turn, followed distribution pattern MMP2. The expression of MMP and TIMP correlated with the location of higher lymphocyte activity and aggressiveness of MF. The activity of MMP2 and MMP9 was higher in tMF compared to more indolent groups.

L-04 IMPACT OF IMMUNODEFICIENCY ON OUTCOMES AND IMMUNE-CHECKPOINT MOLECULE EXPRESSION IN MY-COSIS FUNGOIDES

ORAL Warren S*, Kheterpal M, Moskowitz A, Myskowski PL, Horwitz S, Pulitzer M Memorial Sloan Kettering Cancer Center, New York, USA

INTRODUCTION: Immunodeficiency (ID) is associated with worse outcomes and decreased immune-checkpoint molecule expression in melanoma. Our objective was to determine whether ID has similar associations in mycosis fungoides (MF).

METHODS: We studied 23 MF patients with ID and 17 age/stage/race matched controls with mean follow-up of 4-years, for differences in clinical course, histopathology, and expression of PD-1, PD-L1, FoxP3, and IL-17. ID etiologies included: prior history of other lymphoma (10), recent/current pregnancy at MF diagnosis (7), HIV (1), hypogammaglobulinemia (2) and history of chemotherapy for other cancer (3). Clinical records for 20 ID and 17 control patients were reviewed. Slides were reviewed and immunostains performed on 12 ID patients and 10 controls.

RESULTS: Compared to controls, ID patients were more likely to have treatment failure (TF) (12/20 vs. 5/17, p=0.04) and TF within 3-years of MF diagnosis (11/20 vs. 4/17, p=0.03). ID patients were more likely to show angiocentrism (6/12 vs. 0/10, p=0.005) and larger cell size (1.92±0.51 vs. 1.30±0.48, p=0.009). ID cases were more likely to show >10% PD-1 positivity (9/11 vs. 4/10, p=0.031) and PD-L1 (7/12 vs. 2/10, p=0.042) with a higher average percent PD-1+ cells (43.27±40.22 vs. 11.2±13.62, p=0.028). Differences in survival, LDH, erythroderma, FoxP3 or IL-17 expression or histopathologic features characteristically associated with worse disease, including depth, ulceration, granulomatous changes or syringotropism were not present; there was a trend away from folliculotropism in ID. All cases with TF within 3-years of MF diagnosis trended toward increased PD-1 expression, IL-17 staining intensity, dermal involvement, epidermal hyperplasia and Pautrier's microabscesses, and associated with angiocentrism (5/8 vs. 1/14, p=0.005) and CD4:8 \geq 20:1 (4/4 vs. 1/7, p=0.002) versus patients without TF in that time.

CONCLUSIONS: Immunodeficiency was associated with worse outcomes and increased expression of PD-1 and PD-L1 in MF, suggesting that ID patients with MF may be good candidates for immune-checkpoint inhibitor therapy. Larger studies are needed to validate these findings.

L-05 ROLE OF PAK1 IN THE ONSET AND PROGRESSION OF CUTANEOUS T-CELL LYMPHOMA

ORAL Wang Y*, Zhang C

Department of Dermatology and Venereology, Peking University Third Hospital, Beijing, China

INTRODUCTION: PAK1 is a serine/threonine protein kinases, which regulate cell morphology, motility, survival, and proliferation. Recent evidence showed PAK1 was overexpressed in multiple cancer types including lymphoma. The aim of this study was to investigate the expression pattern of PAK1 in cutaneous T-cell lymphoma(CTCL).

METHODS: Immunohistochemical staining was performed using paraffin-embedded specimens, which were from patients with CTCL and patients with benign inflammatory dermatoses(BID). Immunoreactive score was defined as the product of staining intensity and the percentage of positive cells. Statistical analysis was performed by independent-samples t-test.

RESULTS: Compared with BID, a higher PAK1 expression was detected in CTCL which further increased in atypical lymphocyte. 6 of 8 (75%) cases of CTCL showed moderate staining intensity, 25% cases of CTCL(tumor stage) showed strong staining intensity . However, only 2 of 8(25%) BID showed moderate staining intensity. There was a significant difference between CTCL and BID(p<0.05). CONCLUSIONS: Our study demonstrated the overexpression of PAK1 in CTCL lesions,

suggesting that PAK1 may play an important role in the onset and progression of CTCL and may be a potential therapeutic target for the treatment of CTCL in the future.

Scientific Session L. Applied Research

L-06 DOXYCYCLINE IS AN NF-kB INHIBITOR THAT INDUCES APOPTOTIC CELL DEATH IN MALIGNANT T-CELLS

ORAL Alexander-Savino CV¹, Hayden MS¹, Richardson C², Zhao J³, Poligone B*^{1,4}

¹Rochester General Hospital Research Institute, Center for Cancer and Blood Disorders, 1425 Portland Avenue, Rochester, NY 14621. ²Division of Allergy, Immunology and Rheumatology, University of Rochester School of Medicine, 601 Elmwood Avenue, Rochester, NY 14642, ³ Department of Biomedical Genetics, University of Rochester School of Medicine, 601 Elmwood Avenue, Rochester, NY 14642. ⁴Rochester Skin Lymphoma Center, 6800 Pittsford-Palmyra Rd, Fairport, NY 14450.

INTRODUCTION: Constitutive or aberrant activation of NF-κB, a regulator of immune response and an important participant in carcinogenesis and cancer progression, is encountered in many types of cancer including Cutaneous T-cell Lymphoma (CTCL). This makes NF-κB a potential therapeutic target for this disease.

METHODS: While analyzing gene-expression profiles of a variety of small molecule compounds that target NF- κ B, we discovered the tetracycline family of antibiotics, including doxycycline to be potent inhibitors of the NF- κ B pathway. Doxycycline is well-tolerated, safe, and inexpensive; and is commonly used as an antibiotic and anti-inflammatory for the treatment a multitude of medical conditions. Different cell lines from patients with the two most common subtypes of CTCL, Mycosis Fungoides (MF) and Sézary Syndrome (SS), along with primary CD4+ T-cells from a patient with SS, were treated with doxycycline and the effects of treatment were studied through flow cytometry and western blots.

RESULTS: In our current study, we show that doxycycline induces apoptosis in a dose dependent manner in most CTCL cell lines examined and in primary CD4+ T-cells from a patient with SS. Response to treatment correlated with doxycycline's ability to inhibit TNF induced NF-xB activation. Doxycycline induces cell death through the activation of caspase-8 and the release of cytochrome c, suggesting the involvement of both the extracellular and intracellular pathways of apoptosis. Furthermore, doxycycline's ability to induce apoptosis in CTCL cells can be reversed through the inhibition of reactive oxygen species.

CONCLUSIONS: These results warrant further study on the efficacy of doxycycline in the treatment of CTCL. A clinical trial to study the efficacy and safety of doxycycline in patients with relapsed CTCL is underway. Further study will identify the chemical components of doxycycline that make it a lymphoma killer.

Abstracts * indi

* indicates presenting author

Scientific Session M. Therapeutics 1: Translational/Preclinical Studies

M-01 NOVEL TREATMENT OPTION FOR CTCL: STUDYING THE EFFECTS OF DIMETHYLFUMARATE FROM BENCH TO BEDSIDE

ORAL Nicolay JP*^{1,2}, Müller-Decker K³, Schroeder A², Brechmann M², Möbs M^{4,5}, Maurier N¹, Géraud C¹, Assaf C^{4,6}, Goerdt S¹, Krammer PH², Gülow K²

¹Department of Dermatology, Venereology and Allergy, University Medical Center Mannheim, Ruprecht-Karls-University of Heidelberg, Mannheim, Germany; ²Division of Immunogenetics, German Cancer Research Center, Heidelberg, Germany; ³Core Facility Tumor Models, German Cancer Research Center, Heidelberg, Germany; ⁴Department of Dermatology, Venereology and Allergy, University Medical Center Charité, Berlin, Germany; ⁵Institute of Pathology, University Medical Center Charité, Berlin, Germany; ⁶Department of Dermatology, Venereology and Allergy, HELIOS Klinikum, Krefeld, Germany

INTRODUCTION: Despite intensive efforts in recent years, a curative therapy for cutaneous T cell lymphoma (CTCL) has not yet been developed thus requiring new therapeutic approaches with higher efficacy rates and milder side effects. NFkB-directed therapy would leave bystander T cells widely unaffected while restoring apoptosis in CTCL malignant cells. The purpose of our research is to provide a comprehensive study from bench to bedside on the effects of the NFkB-inhibiting drug dimethylfumarate (DMF) on CTCL in vitro, in vivo in an animal model and in a clinical phase IIA study.

METHODS: We performed in vitro experiments including different methods of cell death measurements as well as mechanistic studies. In addition we used xenograft mouse models to prove the relevance of this data in vivo. Most recently, we started a clinical phase IIA study in which CTCL patients stage IB-IV are treated orally with DMF for 26 weeks. We assess for response to treatment in skin and blood, for quality of life and for immunologic parameters.

RESULTS: We show significant and specific CTCL cell death upon DMF treatment in vitro, from which healthy T cells are almost completely spared. DMF-induced CTCL cell death is mechanistically mediated by downregulation of NF κ B components and suppression of the NF κ B-related anti-apoptotic signalling. In our mouse models, DMF treatment inhibits CTCL tumor growth and spreading to distant sites via NF κ B-related cell death induction. In our clinical study, the first patient with stage IV CTCL showed a dramatic partial remission of the disease with the tumor burden in the blood dropping by >80% and a massive increase in quality of life.

CONCLUSIONS: DMF has proven highly effective in cell death induction that is specifically restricted to CTCL cells and activated T cells in vitro. This effect leads to a reduction of tumor formation and metastasis in vivo in xenograft mouse models. Given these promising preclinical results first clinical study data indicate that these effects also seem to translate into successful clinical CTCL treatment with DMF, although further data from the clinical study are needed to finally confirm these first observations.

M-02 TRANSLATIONAL DEVELOPMENT OF MRG-106, AN OLIGONUCLEOTIDE INHIBITOR OF MIR-155, AS A NOVEL THERAPY FOR CTCL

ORAL Seto AG^{*1}, Beatty XT¹, Tetzlaff MT², Pestano LA¹, Gordon GS¹, Duvic M², Rodman DM^{1, 3}, Marshall WS¹, Jackson AL¹ ¹miRagen Therapeutics, Inc. Boulder, Colorado, USA; ²MD Anderson Cancer Center, Houston, Texas, USA; ³Nivalis Therapeutics, Boulder, Colorado, USA, current affiliation

INTRODUCTION: microRNAs are short, non-coding RNAs that regulate expression of hundreds of genes that impact physiological processes and cellular phenotypes. miR-155-5p is a well-described oncomiR with a strong mechanistic link to cutaneous T-cell lymphoma (CTCL). The objective of this study is to demonstrate activity of MRG-106, an oligonucleotide inhibitor of miR-155, in CTCL cell lines and to identify translational biomarkers for a Phase 1 clinical trial of MRG-106.

METHODS: An LNA-modified oligonucleotide inhibitor of miR-155-5p, MRG-106, was selected based on its ability to de-repress canonical miR-155-5p targets in multiple mycosis fungoides (MF) cell lines in vitro. MRG-106 showed optimal pharmacodynamic activity without additional formulation. In addition to gene expression changes measured by RT-PCR and microarray profiling, the effects of MRG-106 treatment on CTCL cell line growth and the apoptosis pathway were measured biochemically. RNA was extracted from FFPE sections of skin biopsies from patients with patch, plaque, or tumor stage MF lesions followed by quantitation of miR-155-5p expression by RT-PCR. These results were correlated with various clinical characteristics.

RESULTS: MRG-106-mediated inhibition of miR-155-5p in all MF cell lines tested resulted in transcriptome changes consistent with miR-155-5p target gene modulation, reduction in cell proliferation, and activation of the programmed cell death pathway. The gene expression and phenotypic effects were inhibitor dose-dependent and sequence-specific. Expression profiling identified a set of 600 genes common to all responsive cell lines that are both direct and downstream of miR-155-5p. The gene signature is enriched for genes important in cell cycle and apoptosis pathways. Retrospective analysis of 77 skin biopsies from patients with stage I, II, or III MF showed that miR-155-5p levels are highest in tumor-stage lesions, followed by plaque-stage lesions.

CONCLUSIONS: These results support a novel mechanistic approach for treating MF through inhibition of miR-155-5p. We have initiated a first-in-human trial in MF patients. The primary objective of the study is the safety and tolerability of MRG-106. The secondary objective is to characterize the PK profile of MRG-106. The exploratory objectives include endpoints based on the preclinical cell line findings, such as measurements of the 600 gene biomarker signature, neoplastic cell accumulation and apoptosis markers in plaque or tumor stage lesions.

Scientific Session M. Therapeutics 1: Translational/Preclinical Studies

M-03 CHIMERIC ANTIGEN RECEPTOR MODIFIED T CELLS TARGETING CHEMOKINE RECEPTOR CCR4 AS A THERAPEUTIC MODALITY FOR T-CELL MALIGNANCIES INCLUDING CTCL

ORAL Perera LP¹, Zhang M¹, Nakagawa M¹, Petrus MN¹, Maeda M², Kadin ME^{*3}, Waldmann TA¹, Perera PY⁴ ¹National Cancer Institute, Bethesda, MD, USA, ²Institute for Virus Research, Kyoto University, Kyoto, Japan; ³Boston University and Roger Williams Medical Center, Providence RI, USA, ⁴Veterans Affairs Medical Center, Washington D.C, USA

INTRODUCTION: With the emerging success of treating CD19 expressing B cell malignancies with ex vivo modified, autologous T cells that express CD19-directed chimeric antigen receptors (CAR), there is intense interest in expanding this technology to develop effective modalities to treat other malignancies. Exploiting this approach to develop a therapeutic modality for T cell malignancies, we generated a lentivirus-based CAR gene transfer system targeting the chemokine receptor CCR4 that is over-expressed in a spectrum of T cell malignancies as well as in CD4+CD25+Foxp3+T regulatory cells that accumulate in the tumor microenvironment constituting a barrier against anti-tumor immunity.

METHODS: Variable heavy (VH) and variable light (VL) kappa domain sequences of a fully humanized affinity matured anti CCR4 antibody were utilized in the construction of our lentivirus based CCR4 CAR comprised of CD8 derived hinge/transmembrane domain, and 4-1BB (CD137) plus CD3z signaling modules. The cytotoxic effector activity of CCR4 CAR T cells was determined either using both a standard 4-hour ⁵¹Cr release assay and a luciferase based-biophotonic cytotoxicity assay. A luciferase-tagged patient derived adult T cell leukemia cell line was used for in-vivo efficacy assays in NSG mice.

RESULTS: Ex vivo modified, donor-derived T cells that expressed CCR4 directed CAR displayed antigen-dependent potent cytotoxicity against patient-derived cell lines representing ATL, CTCL, ALCL and a subset of HDL all of which express abundant cell-surface CCR4. Furthermore, these CAR T cells eradicated leukemia in a mouse xenograft model of ATL.

CONCLUSIONS: CCR4 directed CAR T cells can be exploited to effectively treat a spectrum of T-cell malignancies for which existing treatment regimens are largely inadequate and do not confer long-term survival.

M-04 DIFFERENTIAL TRANSCRIPTOME RESPONSE IN MYCOSIS FUNGOIDES PATIENTS FOLLOWING SILICON PHTHALO-CYANINE 4 PHOTODYNAMIC THERAPY

ORAL Ahsanuddin S^{1*}, Guan L¹, Suggs A¹, Tacastacas J¹, Oyetakin-White P¹, Selph J¹, Fu P², Leahy P, Lam M^{1,3}, McCormick T^{1,4}, Cooper K^{1,3,4,5}, Baron ED^{1,3,4,5}

¹Department of Dermatology, Case Western Reserve University Hospitals, Cleveland, USA, ²Department of Biostatistics, Case Western Reserve University Hospitals, Cleveland, USA, ³Case Comprehensive Cancer Center, Cleveland, USA, ⁴Case Skin Diseases Research Center, Case Western Reserve University/University Hospitals Case Medical Center, Cleveland, USA, ⁵Dermatology Service, Louis-Stokes VA Medical Center, Cleveland, USA

INTRODUCTION: This report summarizes the results of a phase I trial conducted at University Hospitals Case Medical Center (Cleveland, OH) of Pc 4 photodynamic therapy (Pc 4-PDT) in subjects with stage IA-IIA cutaneous T-cell lymphoma/ mycosis fungoides. Furthermore, we explore a differential transcriptome response to treatment that is associated with varying cardiovascular disease (CVD) risk.

METHODS: A dose escalation schema was used to determine the MTD for a single light exposure following Pc 4 application. To evaluate the molecular mechanisms of single and multiple light exposures in Pc 4-PDT, we used histological assays, Affymetrix HTA 2.0 GeneChip microarrays, BAMarray 3.0 statistical software, and Ingenuity Pathway Analysis (IPA).

RESULTS: Eleven subjects with stage IA/IB mycosis fungoides were enrolled. The MTD for single light exposure was determined to be 0.1 mg/mL of Pc 4 and a fluence of 150 J/cm². Differential gene expression analysis of our microarray data suggested that Pc 4-PDT halts cell cycle progression and induces cell death, corroborating previous in vitro findings. Histologically, significant differences in TUNEL+ apoptosis were observed following treatment (p=0.001). Principal component analysis of microarray data revealed that a CVD risk assessment enabled cohort separation based on gene expression. Differences were seen within these groups in the expression of critical inflammatory and tissue remodeling genes, as well as in the AhR signaling pathway.

CONCLUSIONS: Pc 4-PDT may induce a differential transcriptome response in subjects associated with varying CVD risk. Thus, alternative response mechanisms are important to consider during PDT of CTCL patients.

M-05 PRECLINICAL INVESTIGATION OF SGN-CD70A DRUG-ANTIBODY CONJUGATE IN T CELL LYMPHOMAS

ORAL Yang YC¹, Wang L², Pincus L³, Gill R², Ai W¹*

¹Department of Medicine, Division of Hematology and Oncology, University of California, San Francisco; ²Department of Laboratory Medicine, University of California, San Francisco; ³Department of Dermatology, University of California, San Francisco

INTRODUCTION: CD70 is a member of the TNF superfamily and expressed in a variety of hematologic malignancies. SGNCD70A is a novel antibody-drug conjugate that combines an anti-CD70 monoclonal antibody with a synthetic DNA cross-linking molecule pyrrolobenzodiazepine (PBD) dimer. SGNCD70A is currently under clinical investigation in B cell lymphomas. In this study, we investigated the anti-tumor activity of SGNCD70A in T cell lymphomas.

METHODS: We first examined CD70 expression by IHC in nodal and cutaneous T cell lymphomas using patient biopsy specimens. CD70 expression on tumor cells was examined by two pathologists independently and scored as negative (< 5%), focally positive

Scientific Session M. Therapeutics 1: Translational/Preclinical Studies

(5% to 50%), or diffusely positive (> 50%). Next, we investigated the anti-tumor activity of SGNCD70A in T cell lymphoma cell lines. We treated CTCL cell lines with SGNCD70A at various concentrations, after which growth inhibition and apoptosis were measured by MTT assays and flow cytometry, respectively. The negative control for SGNCD70A in these experiments is h00d-1910, an isotype control of the anti-CD70 antibody conjugated to PBDDescribe your results in a logical sequence.

RESULTS: CD70 expression was observed across all subtypes of PTCL (Table 1). The expression of CD70 in CTCL is presented separately at this meeting.Next, we showed that SGNCD70A potently inhibited cell proliferation in CD70-expressing CTCL lines Hut 78, H9, MJ with a GI50 of 2.4 ng/ml, 3.2 ng/ml and 145.4 ng/ml, respectively; but had no activity in CD70-negative lines. Further, SGNCD70A induced apoptosis in CTCL cell lines with CD70 expression. Currently, we are investigating the anti-tumor activity of SGNCD70A in primary T cell lymphoma cells and xenograft models.

CONCLUSIONS: CD70 is expressed in both nodal and cutaneous T cell lymphomas. SGNCD70A shows promising anti-tumor activity in CTCL cell lines.

Table 1. CD70 expression by IHC in nodal T cell lymphomas					
Histology		CD70 IHC			
riistology	N	Negative (%)	Focally positive (%)	Diffusely positive (%)	
ALCL, ALK+	9	3 (33%)	1 (11%)	5 (56%)	
ALCL, ALK-	6	3 (50%)	0 (0%)	3 (50%)	
PTCL	13	5 (38%)	7 (54%)	1 (8%)	
MF	3	1(33%)	1 (33%)	1 (33%)	
NK/T -L	3	2 (67%)	1 (33%)	0 (0%)	
Total	34	14 (41%)	10 (29%)	10 (29%)	

M-06 CHARACTERIZATION OF CD70 IMMUNOPEROXIDASE STAINING ON CUTANEOUS T-CELL LYMPHOMAS

ORAL Hinds B¹, Ai WZ², McCalmont TH^{3,4}, Pincus LB*^{3,4}

¹Department of Dermatology, University of California, San Diego. ²Department of Medicine, Division of Oncology and Hematology, University of California, San Francisco. ³Department of Dermatology, University of California, San Francisco ⁴Department of Pathology, University of California, San Francisco

INTRODUCTION: CD70 (CD27 ligand) is a member of the TNF superfamily that transiently activates T and B lymphocytes, NK cells, and mature dendritic cells. It is known to be expressed on certain types of systemic lymphomas and solid organ carcinomas. There are currently CD70 antibody-drug conjugates in Phase I Clinical Trials for treatment of these malignancies. Evaluation of CD70 expression in cutaneous T-cell lymphoma (CTCL) has not yet been reported. Therefore, the purpose of this study was to assess CD70 expression by immunehistochemistry on different forms of CTLCs since CD70 could function as a potential therapeutic target of these lymphomas.

METHODS: We evaluated CD70 expression on 10 cases of tumor-stage mycosis fungoides, 7 cases of anaplastic large cell lymphoma, 7 cases of lymphmatoid papulosis, 3 cases of CD30-positive lymphoproliferative disorder, not otherwise specified and 3 cases of T-cell pseudolymphoma. The staining was scored on the following scale: negative (less than 25% of constituent cell expression), focal positivity (25-50% of constituent cell expression), and significant positivity (50-70% of constituent cell expression) and markedly positive (75-100% of constituent cell expression).

RESULTS: Tumor-stage mycosis fungoides stained as follows: 4 cases were negative; 2 showed focal positivity; 3 demonstrated significant positivity and 2 marked positivity. Anaplastic large cell lymphomas stained as follows: 2 cases were negative; 4 showed focal positivity; and 1 marked positivity. The CD30-positive lymphoproliferative disorders, not otherwise classifiable stained as follows: 2 showed focal positivity and 1 demonstrated marked positivity. The lymphamatoid papulosis stained as follows: 4 showed focal positivity and 2 marked positivity. In all types of CTCL, the staining pattern was both cytoplasmic and dot-like in many cases. In all three of the T-cell pseudolymphomas, less than 25% of the lymphocytes labelled with CD70.

CONCLUSIONS: Marked CD70 expression was detected in a subset of every type of CTCL evaluated in this study. Therefore, while CD70 does not hold discriminatory, it has the potential to serve as a therapeutic target in many forms of CTCL.

M-07 SYNERGY OF ROMIDEPSIN AND MECHLORETHAMINE IN CUTANEOUS T-CELL LYMPHOMA

ORAL Patrone CC*1, Sanchez-Martin M², Frattini MG³, Ferrando A², Palomero T², Geskin LJ¹

¹Department of Dermatology, Columbia University Medical Center, New York, NY, USA. ²Columbia University Institute for Cancer Genetics, New York, NY, USA. ³Department of Medicine, Columbia University Medical Center, New York, NY, USA.

INTRODUCTION: Romidepsin, a histone deacetylase inhibitor, and mechlorethamine, an alkylating agent, are two FDA-approved monotherapies for cutaneous T-cell lymphoma. Here we seek to systematically characterize the synergistic interaction of the two

Scientific Session M. Therapeutics 1: Translational/Preclinical Studies

drugs in vitro for their potential synergy in vivo.

METHODS: Four CTCL cell lines SeAx, HH, Hut78, and Hut102 were grown in culture. Each cell line was treated with incremental concentrations of romidepsin (0.1nM-5uM), mechlorethamine (1nm-1mM), and DMSO control to generate single-agent dose response curves and determine the mean inhibitory concentration (IC50) at 24, 48, 72, and 96 hour incubations. To evaluate synergy, cells lines and primary samples were treated with doses 0.25, 0.50, 1, 2, and 4 times the IC50 of the drugs alone and in combination and incubated for 48 hours). Cell viability was assessed with MTT and CellTiter Glo assays. Isobolograms and combination indices (CI) were generated using the median effect method, as described by Chou and Talalay, to assess if the combined drug effects are additive (CI = 1), synergistic (CI < 1), or antagonistic (CI > 1). The degree of apoptosis induced by the drugs in the cell lines was evaluated with Annexin V/7-AAD staining by flow cytometry. Previously banked primary samples from patients with Sézary Syndrome were sorted for CD4+ cells, immunophenotyped for CD3, CD4, CD8, CD26, and CD7 expression, and stimulated with CD3 and CD28 antibodies. Primary samples and cell lines were treated with 1nM romidepsin, 0.25uM mechlorethamine, the combination of the two drug doses, and DMSO controls. Flow cytometry for cell viability was performed with thiazole orange/propidium iodide staining at 24h, 48h, and 72h. RNA sequencing will be performed on the treated primary cells from the 24h incubation to assess differential gene expression.

RESULTS: Romidepsin and mechlorethamine demonstrated synergism with CI < 1 in all 4 cell lines. Apoptosis was increased with combination therapy compared to single agent therapy in cell lines. In primary samples, cell viability of CD4+ cells was reduced by a greater proportion with combination therapy than with each drug alone, showing statistically significant differences at 48h and 72h. Dose response curves of single agents demonstrated that romidepsin's cytotoxic effects increased over longer incubations through 96 hours, and the effect of mechlorethamine plateaued at 48 hours. The 48-hour IC50s were in the nanomolar range for romidepsin and in the micromolar range for mechlorethamine. RNA sequencing data is currently pending.

CONCLUSIONS: This study provides clear demonstration of synergy in the drug combination romidepsin and mechlorethamine for CTCL/Sézary Syndrome in vitro, making a strong argument to test this drug combination in vivo and in clinical trials.

M-08 RAR-ALPHA/RXR SYNERGISM POTENTIATES RESPONSIVENESS IN CUTANEOUS T CELL LYMPHOMA

ORAL Wang L, DeMarco SS*, Peaks MS, Maiorana-Boutilier AL, Chen JM, Crouch MJ, Shewchuk BM, Shaikh SR, Phillips CM, Bridges LC

East Carolina University Brody School of Medicine, Greenville, NC USA and Arkansas College of Osteopathic Medicine, Fort Smith, AR USA

INTRODUCTION: Molecular resolution of how retinoid-based agents resolve cutaneous T cell lymphoma (CTCL) is lacking. The purpose of the study was to identify the specific RAR and RXR nuclear receptor isotypes that transduce retinoid exposure into desired responses (e.g. apoptosis) in CTCL cell lines, and if these isotypes exhibit synergism.

METHODS: A battery of receptor agonists and antagonists, including Bexarotene, were cultured with multiple CTCL cell lines including SeAx, MyLa, HuT78, HuT102 and MJ as well as a control non CTCL cell line, Jurkat. Changes in adhesion, chemotaxis, and viability were determined by a combination of methods including static cell adhesion assays, TransWell chamber assays, apoptotic measurements via flow cytometry, and BrdU proliferation assays. Western blot analysis was utilized to analyze the emergence of apoptotic markers during retinoid exposure.

RESULTS: The data demonstrate that RAR α drives retinoid responses, namely, integrin β 7-dependent adhesion and CCR9-mediated chemotaxis in CTCL cells. Of note, concomitant activation of RAR α and RXR nuclear receptors yielded synergistic increases in adhesion and migration at concentrations where single agents were ineffective. As the established paradigm of retinoid action in CTCL is apoptosis and growth arrest, the role of RAR α /RXR in these events was studied. As with adhesion and migration, RAR α / RXR synergism prompted apoptosis and dampened CTCL cell proliferation at reduced retinoid doses with abbreviated exposure times compared to single agents. Strikingly, RAR α /RXR synergism induced responses from CTCL lines previously reported to be unresponsive to retinoids. Taken together, these data provide a novel framework that may further refine a proven CTCL therapy.

CONCLUSIONS: The current study provides molecular resolution as to which nuclear receptors transduce retinoid exposure into CTCL responsiveness. Our work suggests that Bexarotene therapy can be augmented by combinatorial drug therapy with a RARa agonist to induce synergistic receptor activation. Decreasing the concentration of Bexarotene required to elicit a desired response and increasing the specificity by targeting distinct receptor isotypes would plausibly minimize the adverse side effects (e.g. hyperlip-idemia, hypothyroidism, hypercholesterolemia) commonly associated with retinoid use. The significance of this work is underscored by the historical success of retinoid-based therapies such as Bexarotene and the potential undiscovered therapies still embodied within vitamin A.

M-09 AN-7 SENSITIZES CUTANEOUS T-CELL LYMPHOMA CELL LINES TO DOXORUBICIN VIA INHIBITION OF DOU-BLE-STRAND BREAK REPAIR

ORAL Moyal L*1.², Goldfeiz N^{1,2}, Gorovitz B^{1,2}, Tal E³, Rotem C^{1,2}, Rephaeli A⁴, Tarasenko N⁴, Nudelman A⁵, Hodak E^{1,2} ¹Laboratory for Molecular Dermatology, Felsenstein Medical Research Center, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ²Department of Dermatology, Rabin Medical Center, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ³The David and Inez Myers Laboratory for Cancer Research, Department of Human Molecular Genetics and Biochemistry, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ⁴Laboratory for Pharmacology and Experimental Oncology, Felsenstein Medical Research Center, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv,

87

Scientific Session M. Therapeutics 1: Translational/Preclinical Studies

Israel; ⁵Division of Medicinal Chemistry, Department of Chemistry, Bar Ilan University, Ramat Gan, Israel

INTRODUCTION: The histone deacetylase inhibitors (HDACIs) currently approved for the treatment of cutaneous T-cell lymphoma (CTCL) are of quite limited efficacy when used as single agents, and there is an ongoing search for more potent HDACIs and combination modalities. A previous study by our group showed that the novel HDACI butyroyloxymethyl diethylphosphate (AN-7) had better anti-cancer selectivity and efficiency than SAHA in CTCL cell lines and peripheral blood lymphocytes from patients with Sezary syndrome. Furthermore, AN-7 showed the ability to synergize with doxorubicin, an anthracycline compound that leads to DNA double-strand breaks (DSBs). The aim of the present study was to elucidate the mechanism underlying the toxic synergistic interaction between doxorubicin and AN-7.

METHODS: The effect of AN-7 on doxorubin-induced DSBs was analyzed in MyLa and Hut78 cell lines. DSBs were detected by well-known markers: western blot of phosphorylated H2AX (γH2AX) and phosphorylated KAP1 (p-KAP1) which signal the presence of DSBs; immunofluorescence of γH2AX nuclear foci which mark the sites of DSBs; an alkaline single-cell gel electrophoresis comet assay of the DNA tail moment length which correlates with the level of broken DNA. The direct effect of AN-7 on homologous recombination (HR) DSB repair was analyzed following I-Scel induction of DSBs in U2OS cell line. Flow cytometry was used to quantify GFP-positive cells, and western blot was used to detect the expression of various DSB repair proteins.

RESULTS: The induction of DSBs by doxorubicin was evidenced by an increase in all three markers, and their repair, by the subsequent decline in all markers. The addition of AN-7 did not affect the induction of DSBs by doxorubicin. However, AN-7 inhibited the repair of doxorubicin-induced DSBs via the HR machinery, leaving unrepaired DNA, due to reduction in expression of DBS repair proteins.

CONCLUSIONS: The combination of AN-7 and doxorubicin in CTCL cell lines sustains DSBs by interrupting the DNA repair machinery through suppression of DSB repair proteins. Our data provide the mechanistic rationale for combining AN-7 with doxorubicin or other DNA-damage inducers as a therapeutic modality in CTCL.

M-10 RESMINOSTAT - AN EPIGENETIC APPROACH FOR CTCL MAINTENANCE TREATMENT

ORAL Wulff T, Schrepfer S, Kronthaler K, Hamm S, Borgmann M*, Baumgartner R, Vitt D

INTRODUCTION: Advanced stage CTCL is characterized by a phenotypic plasticity with regard to T helper cell status, switching from Th1 to Th2 status at progression. This switch is associated with epigenetic induced changes in the expression STAT4/STAT6 (Litvinov et al. 2014).

Resminostat is a potent, orally available inhibitor of HDACs, already in phase II clinical development. Resminostat induces changes in gene expression resulting in growth inhibition, modified cell differentiation and enhanced tumor immunogenicity.

The purpose of this study is, to investigate in vitro resminostat's anti-tumoral efficacy against CTCL-derived cell lines and its impact on STAT4/STAT6 expression to support its clinical development in CTCL.

METHODS: Resminostat was tested for its inhibitory potency in cell lines derived from mycosis fungoides (MF, MyLa) and Sézary syndrome (SzS, HuT78). To elucidate the inhibitory mechanism, hyperacetylation as primary effect was assessed by high-throughput bead-based ELISA. Further, cell-cycle distribution and apoptosis induction were determined. Resminostat's impact on the STAT signaling in CTCL cells was investigated by analyzing STAT4/STAT6 expression changes after resminostat treatment.

RESULTS: Resminostat caused dose-dependent growth inhibition in CTCL cells at clinically relevant concentrations. Upon treatment, hyperacetylation of histone-H3 was detected substantiating the epigenetic effect. Resminostat induced apoptosis while only marginally affecting cell-cycle in these cells.

With high STAT6 and low STAT4 expression MyLa cells reflect the Th2-like-phenotype, associated with later disease stages. Treatment of MyLa with resminostat resulted in a dose-dependent increase in STAT4 expression, which is associated with the Th1-phenotype, and a decrease in STAT6 expression, suggesting a switch from the Th2-phenotype to the Th1-phenotype.

CONCLUSIONS: Resminostat displayed in vitro anti-tumor activities both in MF and SzS cells. Regulation of the aberrant STAT signaling on transcription level suggests a stabilization of the less advanced CTCL stage (Th1) or even a reconversion of the advanced Th2 to the Th1-phenotype. Normalizing the epigenetic dysregulation which drives CTCL to progression provides a biological rationale for a maintenance therapy. A clinical phase II trial to evaluate resminostat for maintenance treatment of patients with advanced stage (IIB-IVB) MF or SzS having achieved disease control with systemic therapy is currently in preparation.

M-11 APOPTOSIS INDUCTION IN CUTANEOUS T-CELL LYMPHOMA CELLS AFTER TREATMENT WITH LENALIDOMIDE

ORAL Bakou V¹, Spathis A², Kontsioti F¹, Papageorgiou S¹, Bazani E¹, Vasilatou D¹, Gkontopoulos K¹, Stavroulaki G¹, Glezou I¹, Karakitsos P², Rigopoulos D³, Dimitriadis G¹, Pappa V¹, Papadavid E^{*,3,4}

¹Second Department of Internal Medicine and Research Institute, Attikon University General Hospital, Athens, Greece; ²Department of Cytopathology, Attikon University Hospital, Athens, Greece; ³Second Department of Dermatology, Athens University Medical School, Attikon University General Hospital, Athens, Greece; ⁴Athens University Medical School, A. Sygros Hospital, Athens, Greece

INTRODUCTION: Cutaneous T-cell lymphomas (CTCL) represent a heterogeneous group of extranodal non-Hodgkin lymphomas, derived from skin-homing mature T-cells, with Mycosis fungoides (MF) and Sézary syndrome (SS) being the commonest types, comprising 54% of all CTCL. Since no curative treatment for CTCL is yet available, we investigated the effect of Lenalidomide, an immunomodulatory agent (IMID) with clinical efficacy, among others, in Chronic Lymphocytic Leukemia and Non-Hodgkin's lymphomas,

Scientific Session M. Therapeutics 1: Translational/Preclinical Studies

on cell death of CTCL cell lines. Briefly, describe your methodology.

METHODS: Three CTCL cell lines were used. MyLa, (MF), SeAx and Hut-78 (both SS). Cells were cultured in RPMI 1640 and were treated with various concentrations of Lenalidomide (1μ M, 10μ M and 100μ M) for 24, 48 and 72h. Apoptosis was determined by flow cytometry using the Annexin V/PI method. Describe your results in a logical sequence.

RESULTS: All cell lines responded with enhanced apoptosis at various lenalidomide treatment conditions. Among the three lines, MyLa and SeAx cells were affected the most. Specifically, MyLa cells exhibited a statistically significant augmentation on their apoptosis compared to untreated cells after treatment with 10µM and 100µM Lenalidomide for 24h (9.7 and 8.66 vs 4.83, p=0.000 and p<0,001, respectively) and 48h (6.1 and 4.46 vs 3,36, p=0.000 and p<0,007, respectively), as well as after treatment with 10µM Lenalidomide for 72h (5.3 vs 4.7, p=0.000). Similarly, SeAx cells exhibited high apoptotic rates compared to untreated cells after treatment with 10µM Lenalidomide for 72h (5.3 vs 4.7, p=0.000). Similarly, SeAx cells exhibited high apoptotic rates compared to untreated cells after treatment with 1µM Lenalidomide for 72h (1.5, 2.4 and 7.03 vs 0.13, p=0.000, respectively). Lenalidomide had a rather much more moderate effect on the apoptosis of Hut-78 cells, which presented with enhanced apoptosis compared to untreated cells only after treatment with 1µM Lenalidomide for 72h (1.33 vs 0.8, p>0,009).

CONCLUSIONS: Our observations demonstrate that Lenalidomide leads to enhanced sensitivity to apoptosis in CTCL cell lines. Most importantly, our data indicate that low concentrations of Lenalidomide (1µM and 10µM) are more effective in terms of apoptosis induction in CTCL. Although these initial results need to be further confirmed both in vitro and in vivo, they appear very encouraging for the integration of Lenalidomide treatment, alone or in combination, in CTCL therapy.

M-12 TARGETING CK1 EPSILON AS A NOVEL THERAPEUTIC STRATEGY IN C-MYC DRIVEN LYMPHOMA

ORAL Deng C^{*1,2,3}, Lipstein MM², Scotto L², Jirau Serrano X², Mangone MA², Li S³, Vendome J⁴, Hao Y⁵, Xu X², Deng SX², Horstein N⁴, Tatonetti NP⁵, Lentzsch S³, Sims P⁴, Honig B⁴, Landry DW², O'Connor OA^{1,2}

¹Center for Lymphoid Malignancies, ²Division of Experimental Therapeutics, ³Division of Hematology & Oncology, Department of Medicine; ⁴Department of Systems Biology, ⁵Department of Biomedical Informatics, New York, NY, USA

INTRODUCTION: The oncogene c-Myc has been recognized as an "undruggable" target for over three decades. The goal of the current study is to develop novel strategies for targeting of c-Myc. c-Myc is a master transcription factor and one of the most frequently altered genes across a vast array of human cancers including cutaneous T cell lymphoma (CTCL), and is thus an attractive therapeutic target. However, no direct inhibitor of c-Myc has been successfully developed for the treatment of any cancer. Cancer cells use a number of mechanisms to ensure elevated expression of c-Myc, for example, through mTOR mediated hyper-phosphorylation and thereby inactivation of the translation "brake", 4E-BP1. CK1 epsilon is a poorly understood kinase and is recently implicated in phosphorylating 4E-BP1 independently of mTOR. However, no drug targeting CK1 epsilon is available for the clinic. The goal of the current study is to evaluate a newly discovered CK1 epsilon inhibitor, TGR-1202, in preclinical models of CTCL and other lymphoma.

METHODS: Cytotoxicity was studied in lymphoma cell lines, including CTCL, and primary lymphoma cells using Cell TiterGlo (Promega®). The Bliss additivism model was used to determine the expected inhibition of cell growth and the excess over Bliss (EOB) values. EOB values above 0 indicate synergy, with higher values indicating higher levels of synergy. Expression of c-Myc was investigated at the translation and transcription levels, using a combination of Western blot, qPCR, and a bi-cistronic lucifer-ase reporter we developed to study cap dependent translation. Gene expression profiling (GEP) studies were conducted using RNAseq, and analyzed by the Fisher t-test and running enrichment score (RES) between different treatment groups. Mechanisms of synergy were determined through interrogating the effects of small molecule inhibitors and shRNA targeting regulators of various regulators of 4E-BP1. Furthermore, translation control was investigated using ribosome profiling. Structural studies of TGR-1202 were performed by in silico docking, and validated by synthesis of novel analogs of TGR-1202. Activity of TGR-1202 on CK1 epsilon was studied by kinome profiling (Reaction Biology®), cell free kinase assay of CK1 epsilon (Promega®), and cell based assay of CK1 epsilon autophosphorylation.

RESULTS: We found that a novel PI3K delta isoform inhibitor TGR-1202, unexpectedly demonstrated activity against CK1 epsilon. Co-targeting of PI3K delta and CK1 epsilon was required to efficiently inhibit phosphorylation of 4E-BP1 and repress expression of c-Myc protein in lymphoma cells. Novel analogs of TGR-1202 demonstrated superior activity in targeting 4E-BP1 and c-Myc. TGR-1202, but not the approved PI3Kdelta inhibitor idelalisib, was highly synergistic with the proteasome inhibitor carfilzomib in CTCL and other lymphoma models. TGR-1202 and carfilzomib (TC) synergistically inhibited phosphorylation of 4E-BP1, leading to suppression of c-Myc translation and silencing of c-Myc dependent transcription. The synergistic cytotoxicity of TC was rescued by overexpression of eIF4E or c-Myc. Furthermore, ribosome profiling demonstrated that the synergistic TC combination preferentially repressed the translation of ribosomal components and genes involved in mitochondrial function and translation initiation.

CONCLUSIONS: These results suggest that TGR-1202 is a first-in-class dual PI3Kdelta/CK1epsilon inhibitor with a distinct activity in silencing gene translation, specifically that of c-Myc. As TGR-1202 has demonstrated promising clinical activity and an excellent safety profile in phase I/II clinical trials in lymphoma, it may be an excellent tool for therapeutic targeting of c-Myc in CTCL and other c-Myc driven cancers.

Abstracts * indic

* indicates presenting author

Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation

N-01 LONG-TERM OUTCOME OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PATIENTS WITH MYCOSIS FUNGOIDES AND SÉZARY SYNDROME

ORAL Onida F*, Saporiti G, Alberti-Violetti S, Soverini G, Motta B, Tagliaferri E, Vincenti D, Corti L, Cortelezzi A, Berti E Onco-hematology and Dermatology Units, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico - University of Milan, Italy

INTRODUCTION: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) currently represents the only curative strategy in selected patients with advanced stage mycosis fungoides (MF) and Sézary syndrome (SS). Reduced intensity conditioning (RIC) regimens have been shown to reduce transplant-related mortality leading to better outcomes in comparison to myeloablative ones. METHODS: As of July 2016, in our Center 36 patients underwent RIC allo-HSCT. Donors were HLA-identical sibling in 16, fully-matched unrelated in 8, 1/2 mismatch-unrelated in 10 and haploidentical sibling in 2. Median age was 53 years (range 19-66). All patients (23 M and 13 F) had stage IIB/IV refractory MF (n=24) or refractory SS (n=12). Median number of previous treatment lines was 6 (range 2-12). Source of stem cells was peripheral blood in 31 patients, bone marrow in 4 and cord blood in 1. Median time from diagnosis to HSCT was 48 months (range 13-264). Conditioning regimens included FC/TBI200, pentostatin+TBI200, and fludarabine/melphalan.

RESULTS: Acute GvHD occurred in 16 patients out of 28 evaluable (57%), grade III-IV in 8 (28%), whereas chronic GvHD was observed in 9 patients (32%), extensive in 3. Following transplantation, a complete remission (CR) was achieved in 22 out of the 33 evaluable patients (67%), of whom 2 experienced relapse at +25 and +35 months, respectively. At the last follow-up, 19 patients were alive and 17 (89%) maintained CR after a median follow-up of 56 months (range 1-185). Out of the 11 patients who did not achieve CR, 10 died from progressive disease (median follow-up of 12 months, range 3-31), while 1 is still alive with disease 37 months after transplant. Transplant-related death occurred in 6 patients (17%), of whom 4 were in CR. In the whole population, the 5-year overall survival was 57% and the 5-year disease-free survival (DFS) was 48%. However, when MF and SS were analyzed separately, 5-yrs DFS were 40% and 88%, respectively (Fig.1). Apart from diagnosis, outcome was primarily associated with status of disease at transplantation.

CONCLUSIONS: Long-term follow-up confirmed favourable outcome of allo-HSCT in patients with advanced-stage CTCL, with extremely encouraging results in SS



N-02 ALLOGENEIC STEM CELL TRANSPLANTATION IN REFRACTORY MF/SS: RESULTS WITH REDUCED INTENSITY CON-DITIONING REGIMEN

ORAL Foss F*, Girardi M, Wilson L, Roberts K, Seropian S Yale University School of Medicine

INTRODUCTION: Allogeneic transplantation has been a curative modality for patients with advanced lymphoma. There is limited data on the role of reduced intensity transplantation in patients with advanced cutaneous T cell lymphomas. Several retrospective series have reported OS and PFS of 40-50% in patients with both MF and SS.¹⁻³ In a review of the CIBMTR registry, Lechowicz et al reported a progression free survival of 31% at one year with no difference in outcomes between ablative and reduced intensity regimens.⁴

METHODS: We report our results from 15 consecutively treated patients with MF/SS who underwent reduced intensity allogeneic transplantation using a pentostatin or fludarabine based reduced intensity regimen. Patients selected for transplant had advanced or refractory folliculotropic or tumor stage MF, patients with large cell transformation (LCT) or SS refractory to multiple systemic regimens. Three patients had folliculotropic MF, 5 had erythroderma and Sezary Syndrome, and 7 had tumor stage disease or large cell transformation. The median age was 51; 4 patients were age 40 or younger. The median time to transplant was 3 years (range 1-7 years). Eleven of 15 had EPOCH chemotherapy for disease control prior to transplantation. All but one patient had CR or minimal residual disease at transplant. Unlike results from other centers using non-TBI containing regimens, in our series 11 of 15 patients received TBI (1200 cGy in 3, 600 cGy in 8). Conditioning regimens included infusional pentostatin / total skin electron beam irradiation/600 cGy TBI in 8, fludarabine/ busulfan in 4, and Cytoxan/ 1200 cGy TBI in 3.

RESULTS: Acute GVHD grade III or IV occurred in 6 patients and extensive chronic GVHD in 6. At a median follow up of 5 years, 10

Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation

patients (66%) are alive, including 3 with LCT, 3 with folliculotropic MF, and 4 with SS. Five patients died, one from AGVHD and 4 from PD. Five patients had recurrence and were treated with a number of agents, including radiotherapy, gemcitabine, brentuximab, pralatrexte, and donor lymphocyte infusions. Of the 5 patients with recurrent disease, 2 had acute skin GVHD and 4 had chronic extensive GVHD. In this small series, there was no association between incidence of GVHD and disease recurrence. At a median follow up of 3 years, 7 patients (46%) remain in remission. Six of 7 had TSEB for skin debulking as part of their transplant conditioning. Our results are similar to Hosing et al, who reported that 20 of 47 patients are alive and free of disease after reduced intensity conditioning. Our regimen is unique in that it included reduced dose TBI, but our similar outcomes suggest that the unlike TSEB, the potential debulking effect of TBI in the reduced intensity regimen did not contribute significantly to overall disease control. CONCLUSIONS: We conclude that reduced intensity allogeneic transplantation with TSEB as a debulking modality is associated with graft-vs-lymphoma effect in patients with SS, LCT, and refractory folliculotropic MF and should be considered for high risk patients who are candidates for transplant.

N-03 PRALATREXATE IN CUTANEOUS T CELL LYMPHOMA: RETROSPECTIVE EXPERIENCE WITH AND WITHOUT LEUCOV-ORIN

ORAL Anlong L, Girardi M, Parker T, Foss F* Yale University School of Medicine

Pralatrexate (PDX, Folotyn®) is a folic acid analog designed to preferentially accumulate in cancer cells via the reduced folate carrier and acts as an antimetabolite interfering with DNA synthesis leading to cell death. In a clinical trial of pralatrexate in relapsed and refractory mycosis fungoides (MF) and Sezary Syndrome (SS), the overall response rate was 45%, the median cycles were 4 (range 1-23) and the optimal dose was defined as 15 mg/m2 weekly x 3 every 4 weeks.¹ We reviewed our experience with Pralatrexate in 27 consecutively treated patients with relapsed and refractory MF/SS. The median age was 54 (range 27-89). Two had Stage IIA, 12 had Stage IIB, 3 had Stage III and 10 had Stage IV disease. The starting dose of Pralatrexate was 15 mg/m2 except in patients with impaired performance status or mild renal insufficiency, who had a starting dose of 10 mg/m2 with dose escalation as tolerated by toxicity. The median cycles were 5 (range 2-33). The overall response rate (CR+PR) was 57% with 2 CR and 13 PR. Response rate in Stage IIB was 50% and in Stage IV was 70%. ORR was similar in patients treated with <15 mg/m2 (40%, n=15) and those treated at > 15 mg/m2 (n=12). Six patients experienced disease stabilization for overall disease effect in 21 of 27 patients, and these patients remained on therapy for 11-33 months. The addition of Leucovorin to Pralatrexate in the last 12 consecutively treated patients significantly reduced the incidence of mucositis from 47% to 17%. Skin flare occurred in 16 of 27 patients and occurred with the same frequency in the presence or absence of Leucovorin. In conclusion, we report a high overall response rate for Pralatrexate in tumor stage and Stage IV MF/SS, similar to that reported by Horwitz et al. We demonstrate that with the addition of Leucovorin to ameliorate mucositis, overall disease benefit was seen in up to 77% of patients. ¹Horwitz et al, Blood 2012, 119(18), 4115-22.

N-04 LOW DOSE TOTAL SKIN ELECTRON BEAM THERAPY (TSEB) 12GY IN 8 # OVER 2 WEEKS. THE RESULTS IN 103 PATIENTS FROM THE UK

ORAL Morris SL¹, Scarisbrick JJ², Frew J³, Irwin C², Grieve R², Kuciejewska A¹, Bayne S¹, Child F¹, Wain M¹, Whittaker S¹ ¹Guys and St Thomas, London, ²University Hospital Birmingham, ³Freeman Hospital, Newcastle upon Tyne

INTRODUCTION: The standard 30Gy dose schedule of TSEB is a very effective treatment with high response rates and duration of response (DOR) in patients with Mycosis Fungoides (Stage IB CR 59% median DOR 18 months, Stage IIB CR 47% median DOR 9 months) Following reports of similar durations of response to lower doses of TSEB a low dose schedule of TSEB was introduced in the UK.

METHODS: A 2-week protocol of 12Gy in 8 fractions over 2 weeks was agreed, using the Stanford technique. Data was collected prospectively using the EORTC/ISCL endpoints, and the new endpoint duration of clinical benefit (DoCB). Toxicity was scored according to the CTCAEv4.0.

RESULTS: 103 patients received treatment between 2011 and 2016 with a median follow up of 20.6 months (range 3.3 to 53 months). 54 patients were stage IB, 33 stage IIB, 12 stage II and 4 stage IV. The median age was 68 (range 26 – 91). The CR was 18%, PR 69%, SD 8% and 5% progressed on treatment (stage IB CR 20%, PR 74%, SD 6%, stage IIB CR 21%, PR 76%, SD 1%, stage III CR 8%, PR 42%, SD 33%, stage IV CR 0%, PR 25%). In the patients who had a CR the median freedom from relapse was 7.3 months (14.6 months in stage IB and 4.7 months in stage IIB). The median DOR was 11.7 months (stage IB 15.4 months, stage IIB 10.0 months, Stage III 10.6 months, stage IV 2.4 months). The median DoCB was 18.8 months (stage IB 27.2 months, stage IIB 14.2 months, stage III 1.97 months, stage IV 4.4 months). The treatment was well tolerated. Grade 2 toxicities included: fatigue 8%, Leg oedema 4%, Blisters 2%, radiation dermatitis 12% and skin infection 5%.

CONCLUSIONS: Low dose 12Gy TSEB is well tolerated and has a similar high overall response rate and a similar duration of response compared to 30Gy.

N-05 THE FRENCH EXPERIENCE OF CHLORMETHINE GEL FOR THE TREATMENT OF MYCOSIS FUNGOIDES: A RETRO-SPECTIVE SERIES OF 107 CASES

ORAL Mathieu S*1, Ram-Wolff C, Beylot-Barry M², D'Incan M³, Oro S⁴, Quéreux G⁵, Chaby G⁶, Aubin F⁷, Hainaut Wierzbicka E⁸, Sko-

Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation

wron F⁹, Bonnet N¹⁰, Dereure O¹¹, Adamski H¹², Brunet-Possenti F¹³, Bagot M¹, Groupe Français d'Etude des Lymphomes Cutanés (GFELC)

¹Hôpital Saint-Louis, APHP, Paris, France; ²CHU Bordeaux, Bordeaux, France; ³CHU Clermont-Ferrand, Clermont-Ferrand, France; ⁴CHU Henri Mondor, APHP, Créteil, France; ⁵CHU Nantes, Nantes, France; ⁶CHU Amiens, Amiens, France; ⁷CHU Besançon, Besançon, France; ⁸CHU Poitiers, Poitiers, France; ⁹CH Valence, Valence, France; ¹⁰Hôpital Nord, Marseille, France; ¹¹CHU Montpellier, Montpellier, France; ¹²CHU Rennes, Rennes, France; ¹³Hôpital Bichat-Claude-Bernard, APHP, Paris, France

INTRODUCTION: Chlormethine gel (CG) 160µg/g is an alkylating agent used for the treatment of stage IA, IB or IIA mycosis fungoides (MF). We report 107 cases of cutaneous T cell lymphoma (CTCL) treated with CG, describe adverse effects (AE) and efficacy. METHODS: Members of the « Groupe Français d'Etude des Lymphomes Cutanés » (GFELC) completed questionnaires regarding patients using CG from December 1st 2014 to December 31st 2015.

RESULTS: 64 men (60%) and 43 women (40%), average age 62, were included in this retrospective multicentric study involving 13 French hospitals. 53 patients (50%) had stage IA MF, 40 IB (37%), 6 IIA (6%) and 8 another CTCL (7%). CG was applied 3 days/week (d/w) by 85% of patients (91/107), 1 to 2 d/w by 7% (7/107) and 5 to 7 d/w by 8% (9/107). 77% of cases (82/107) associated dermocorticoids (DC) to CG. AE were reported in 43 cases (40%), mainly contact dermatitis (CD) in 40 cases (37%) resolving promptly with discontinuation of treatment. Complete remission (CR) occured in 7 cases (7%), partial remissions in 53 (50%), stable disease in 21 (20%) and progression in 12 (11%). For 12 cases (11%), data was unavailable. Efficacy of 74% was noted in patients treated > 180 days. On December 31st 2015, 50% of patients (54/107) still used CG, 40% (43/107) stopped (6% of CR, 21% CD, 12% progression and 1% a pregnancy wish). For 9% (10/107) of cases, data was unavailable. Average treatment duration was 162 days. Our study is comparable to an American multicentric randomized controlled study of 260 cases published in 2013 by Lessin et al. reporting no serious AE. CD was reported in 20% of cases, versus 23% in our study even though our application frequency was inferior. Their response rate was comparable to ours (59% versus 57%) and 77% versus 74% for patients treated > 6 months.

CONCLUSIONS: CG is a new topical treatment option for MF. It is well tolerated and shows efficacy. CD is frequent.

N-06 EXTRACORPOREAL PHOTOPHERESIS ASSOCIATED TO MULTIMODAL THERAPY FOR T-CELL CUTANEOUS LYMPHO-MA

POSTER Silva MM^{1*}, Machado JRS¹, Arcuri L J¹, Lermontov S¹, Gonzaga Y¹, Menezes RF¹, Aquino II¹, Araújo RC¹, Bouzas LF¹, Sanchez JA²

¹Instituto Nacional do Câncer, ²Universidade de São Paulo, Brazil

INTRODUCTION: The treatment of mycosis fungoides and Sézary syndrome is primarily determined by disease extent and the impact on quality of life, prognostic factors, and patient age/comorbidities. Advanced stage MF/SS (stages IIB-IVB) is often treatment refractory and results in an unfavorable prognosis; treatment is aimed at reducing the tumor burden, delaying disease progression and preserving quality of life. The goal of this study was to evaluate the clinical response rate of patients with Sézary syndrome and mycosis fungoides to multimodality immunomodulatory therapy consisting of extracorporeal photopheresis in combination with interferon-alfa, retinoids, systemic steroids and/or phototherapy.

METHODS: Multimodality immunomodulatory therapy was used associated to extracorporeal photopheresis in 14 patients with CTCL between August 2007 and January 2016.

RESULTS: From 14 patients treated with multimodality therapy 10 present Sézary syndrome, three erythrodermic mycosis fungoides, one with folliculotropic mycosis fungoides were treated with extracorporeal photopheresis. An overall clinical response of 50% was achieved with multimodality immunomodulatory therapy. Thirty six percent of patients exhibited a complete response, characterized by no evidence of cutaneous disease and a Sézary count less than 5%. Fourteen percent exhibited a partial response. Twenty eight percent were non-responders. Three patients were considered early for evaluation (two dead before 24 cycles and one is beginning extracorporeal photopheresis).

CONCLUSIONS: Based on our experience, multimodality immunomodulatory therapy is an effective treatment for CTCL-poor-responders patients or those with high tumoral charge. The durability of response and impact on overall survival remains to be determined; however, this approach offers an appealing alternative to treatments associated with higher morbidity rates.

N-07 EXTRACORPOREAL PHOTOPHERESIS IN THE TREATMENT OF ERYTHRODERMIC CUTANEOUS T-CELL LYMPHOMA: A SINGLE CENTRE LONG TERM EXPERIENCE

POSTER Just U*, Porkert S, Jonak C, Knobler R

92

Department of Dermatology, Medical University of Vienna, Austria

INTRODUCTION: The present study describes our experience with ECP alone or in combination with interferon-alpha (IFNα), PUVA, total skin electron beam (TSEB), steroids and chlorambucil in treating CTCL patients over a period of 25 years.

METHODS: 26 patients with CTCL treated over a period of 25 years were evaluated in a retrospective manner. Multiple standard clinical and laboratory findings usually identified as indicators for response to treatment were evaluated. Age at disease onset, time elapsed before treatment and clinical stage were included. Analysis encompassed erythroderma, WBC, LDH, and CD4/CD8 ratio. RESULTS: At the time of diagnosis of CTCL mean patient's age was 58.6 years (range 37-78). Male to female ratio was 1.25:1. All 26 patients received ECP for more than 10 cycles. The mean number of ECP cycles was 54.2 (range 14-148 cycles). Overall survival

Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation

rates were estimated by Kaplan Meier method and compared using log-rank tests. A reduction of specific laboratory parameters correlated with response to treatment.

CONCLUSIONS: Patients with CTCL receiving ECP treatment with or without combination of immune-modulatory therapy experience higher response rates and longer survival than controls. Our study suggests that the use of Extracorporeal Photopheresis can have a significant positive effect on survival of a subset of CTCL patients.

N-08 CD209⁺ MONOCYTE-DERIVED MYELOID DENDRITIC CELLS WERE INCREASED IN PATIENTS WITH LEUKEMIC CUTA-NEOUS T-CELL LYMPHOMA AFTER EXTRACORPOREAL PHOTOPHERESIS

POSTER Austin M, Langridge T, Zhang X, Shiue L, Duvic M, Ni X*

Department of Dermatology, the University of Texas MD Anderson Cancer Center, Houston, Texas, USA

INTRODUCTION: Our previous study found that numbers of myeloid dendritic cells (mDC) and their HLA-DR expression were increased after extracorporeal photopheresis (ECP) in patients with leukemic cutaneous T-cell lymphoma (L-CTCL). To further define the subset of ECP-affected mDCs, we assessed the expression of CD209 on mDCs in L-CTCL patients over a 6-month ECP treatment course. It is known that CD209 or DC-SIGN, a transmembrane receptor, is predominantly expressed on monocyte-derived mDCs (Mo-mDC), and can be used as a biomarker for Mo-mDCs.

METHODS: Nineteen L-CTCL patients who started ECP therapy with the CELLEX photopheresis system were enrolled in the study. The peripheral blood was collected at baseline, at Day 2, 1-month, 3-months, and 6-months after initial ECP treatment, and mDC populations as well as CD209⁺ mDC subsets were assessed by multi-color flow cytometry.

RESULTS: At baseline, about one third of patients had low numbers of mDCs, but all patients had lower than normal CD209⁺ mDC counts. The average percentage of CD209⁺ mDCs was 0.064% out of peripheral blood mononuclear cells (PBMC) in normal donors (n=3), but only 0.006% out of PBMCs in patients (n=19, p<0.05). The CD209⁺ mDC subset accounts for about 66.2% of total mDCs in normal donors compared to only 13.9% in patients (p<0.05). Eight patients finished the 3 and/or 6-month treatment course, with 5 clinical responders and 3 non-responders. The average absolute CD209⁺ mDC counts in 8 patients were increased by about 3-fold at 3 months and 2-fold at 6 months post-ECP. The average percentages of CD209⁺ mDCs in PBMCs increased from 0.008% at baseline to 0.015% at 3 months and were unchanged at 6 months. CONCLUSIONS: Our results suggest that patients with L-CTCL have a deficiency in monocyte-derived myeloid dendritic cells which may be attributed to the suppressed immunity. ECP may work by increasing monocyte-derived myeloid dendritic cells and improving anti-tumor immunity in patients with L-CTCL.

N-09 LATE RELAPSE OF CTCL AFTER ALLOGENEIC STEM CELL TRANSPLANT: SUCCESSFUL TREATMENT WITH LOW DOSE INTERFERON ALPHA AND PHOTOPHERESIS

POSTER Spaccarelli N¹, Nasta SD², Cornejo CM¹, Clark R³, Vittorio C¹, Rook AH¹, Kim EJ^{*1}

¹Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA. ²Abramson Cancer Center, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA. ³Department of Dermatology, Brigham and Women's Hospital, Harvard University, Boston, MA, USA.

Hematopoietic stem cell transplantation (HSCT) is a potentially curative therapeutic option for patients with advanced stage cutaneous T-cell lymphoma (CTCL) but has significant risks of transplant related mortality and post-transplant disease relapse. The most frequently reported treatments of post-transplant CTCL relapse are tapering of immunosuppression and donor lymphocyte infusion, which can enhance graft vs tumor effect but have a risk of triggering graft vs. host disease (GVHD). We report a 67 yearold female with Stage IVA₁ Sézary Syndrome/CTCL diagnosed in 2003, refractory to multiple therapies, who underwent matched unrelated non-myeloablative allogenic HSCT in 2010 with complete response and no GVHD. She remained in remission off all immunosuppression until 2013 when she relapsed (T4N0M0B2, no transformation) despite full donor engraftment. Her relapsed CTCL progressed despite donor lymphocyte infusion, romidepsin, pralatrexate, and gemcitabine. In late 2014, she was started on low dose interferon alfa and monthly extracorporeal photopheresis (had previously been on these pre-transplant) and after 6 months achieved complete response (confirmed by high throughput T-cell receptor sequencing of peripheral blood). She remains in remission on this regimen for the past 1.5 years without evidence of acute or chronic GVHD. Late relapses of CTCL after allogeneic HSCT occur and the optimal sequence of treatments for relapsed CTCL remains uncertain. Our patient's relapse did not respond to DLI and multiple single agent chemotherapies, but did surprisingly respond to low dose interferon alpha and extracorporeal photopheresis, possibly through graft vs tumor effect.

N-10 LONG-TERM CLEARANCE OF BLOOD AND MARROW INVOLVEMENT FOLLOWING GRAFT FAILURE AND AUTOLO-GOUS RECONSTITUTION IN A PATIENT WITH SÉZARY SYNDROME WHO UNDERWENT ALLO-SCT

POSTER Saporiti G*, Motta B, Alberti-Violetti S, Tagliaferri E, Vincenti D, Soverini G, Corti L, Cortelezzi A, Berti E, Onida F Onco-hematology and Dermatology Units, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico - University of Milan, Italy

INTRODUCTION: Clinical course of Sezary syndrome (SS) is generally aggressive, with only 25% of patients surviving beyond 5 years from diagnosis. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is currently the only curative treatment option. METHODS: On 06/2008 a 53 y-old gentleman was diagnosed with MF and treated with phototherapy until 04/2011, when lymphocytosis occurred and a Sezary clone was detected by flow cytometry (CD4+,CD7+,CD26-) both in peripheral blood and in marrow.

Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation

A total body CT scan was negative for lymphadenophaties and visceral involvement. ECP was performed from 04/2011 to 04/2013 achieving partial response. On 06/2013, following a non-myeloablative (NMA) conditioning regimen including pentostatin 4 mg/ msq (day -10 and -3), TBI 200 cGy and ATG 7,5 mg/kg, the patient underwent allo-SCT from a 9/10 HLA unrelated male donor. GvHD prophylaxis included cyclosporine and mycophenolate mofetil.

RESULTS: In the early phase the patient showed progressive neutropenia complicated by an Acinetobacter iwoffi bacteremia on day +14.On the following days, leukocyte count continued to decrease; a bone marrow examination performed on day +24 failed to show the presence of engraftment at chimerism analysis, but showed 23% of infiltrate with aberrant phenotype (CD4+, CD7+, CD26-). On day +28 graft failure was confirmed and immunosuppressive therapy was discontinued. Autologous neutrophils (>500/mmc) and platelet recovery (>50000/mmc) were observed on days +45 and +32, respectively. The diffuse skin lesions remained stable during the whole transplant period. Following discharge, regular outpatient visits and blood/marrow examination showed normal CBC counts with persisting lymphocytopenia (<1000/mmc) in blood and no Sezary cells. On 05/2014, due to cutaneous progression, 36 Gy TSEB was administered achieving a VGPR. At the last follow up visit on 06/2016, the patient was still in blood and marrow CR with minimal skin disease.

CONCLUSIONS: Because allogeneic graft failure is normally associated with disease progression, this case appears to be thought-provoking with regard to its correct interpretation, suggesting immunological mechanisms as the responsible for both graft rejection and the long-term clearance of blood involvement.

N-11 PRIMARY CUTANEOUS LARGE CELL ANAPLASTIC LYMPHOMA: THE ROLE OF BRENTUXIMAB WHEN THE OUT-LOOK IS POOR

POSTER Murray DJ*1, Amel-Kashipaz R², Bindu V², Chaganti S³, Shah F⁵, Stevens A⁴, Scarisbrick JJ⁵

¹Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom; ²Department of Histology, University Hospitals Birmingham, Birmingham, United Kingdom; ³Department of Haematology, University Hospitals Birmingham, Birmingham, United Kingdom; ⁴Department of Oncology, University Hospitals Birmingham, Birmingham, United Kingdom; ⁵Department of Dermatology, University Hospitals Birmingham, Birmingham, United Kingdom

INTRODUCTION: Primary Cutaneous Large Cell Anaplastic lymphoma (PC-LCAL) is an orphan disease generally seen to have a good prognosis. We retrospectively collected biological, disease and response data on our patients with PC-LCAL, focusing on usage of the CD30-specific conjugated antibody, brentuximab.

METHODS: The cutaneous lymphoma database at a large supraregional clinic was queried, returning 16 patients with PC-LCAL who received a total of 34 treatments. Biological, disease-specific and treatment-related data were retrospectively collected. Patients received radiotherapy (12), cyclophosphamide/vincristine/doxorubicin/ prednisolone(CHOP) (6), brentuximab (4), methotrexate (4), allogeneic bone marrow transplant (allograft) (2) and other treatments (6).

RESULTS: Overall survival was 72% at 5 years, progression-free survival was 33% at 5 years. The median number of treatments received by each patient was 1 (range 0-7). Radiotherapy had the highest overall response rate (ORR) of 83%. CHOP had an ORR of 83% and a complete response rate (CRR) of 33%. Brentuximab had the highest CRR of 50%. Progression free survival was significantly worse for second and subsequent lines of treatment compared to first line (2.8 months versus 3.8 years p = 0.02 log-rank test). Three patients had disease with an aggressive course. These patients all received systemic high-intensity chemotherapy, followed by brentuximab, and two patients proceeded to allograft. Brentuximab was used in both cases as a successful bridge to achieving a response prior to transplant. One patient relapsed following allograft and was successfully re-treated with brentuximab which maintained disease control for three months prior to succumbing to a chest infection. The other patient is alive and well.

CONCLUSIONS: While PC-LCAL for the majority of patients will have an indolent course, there is a significant fraction of patients who will progress rapidly with an aggressive disease. These patients need to be identified early for referral to haematology and consideration of intensive chemotherapy and allograft. Brentuximab was effective in achieving a robust remission prior to transplant, and also demonstrated a response with re-treatment following relapse.

N-12 BRENTUXIMAB VEDOTIN IN CD30+ CUTANEOUS LYMPHOMA: HOW DO WE TREAT - HOW SHALL WE TREAT?

POSTER Stranzenbach R^{*1}, Dippel E², Schlaak M³, Stadler R¹

¹Department of Dermatology, Johannes Wesling Medical Centre, University Hospital of Ruhr- University Bochum, Germany; ²Department of Dermatology, Klinikum Ludwigshafen, Skin Cancer Center Rheinpfalz, Germany; ³Department of Dermatology and Venereology, University of Cologne, Germany

INTRODUCTION: Brentuximab vedotin is an antibody–drug conjugate that selectively delivers the antimicrotubule agent monomethyl auristatin E into CD30-expressing cells. Some prior studies could demonstrate good efficacy in cutaneous lymphomas. The standard therapeutic scheme is 1.8mg/kg every 3 weeks which is identically to the FDA approved scheme in Hodgkin lymphoma and systemic anaplastic large cell lymphoma. Background of this work is the fact that cutaneous lymphoma have a different pathophysiology and another dynamic than systemic lymphoma. This work should emphasize that there are no existing dose finding studies as rationale for an optimal dosage and interval for cutaneous CD30+ lymphomas. Furthermore we will emphasize that a therapeutic scheme with lower dose and prolonged intervals is also possible but with less side effect and no loss of response. METHODS: Analyzing a case series consistent of 7 patients and conduction of a systemic literature review.

RESULTS: We analyzed a case series of 7 Patients with CD30+ cutaneous lymphoma and who underwent a therapy with brentuximab

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Scientific Session N. Therapeutics 2: Advanced Therapies, incl. HSC Transplantation

vedotin. The start schemes were in all cases 1.8mg/kg. The objective overall response rate were 100% (7of 7 patients). (CR 57%; 4 of 7 patients, PR 43%; 3 of 7 patients). Dose reduction to 1.2mg/kg and prolonged intervals could be performed in some individuals without loss of effect. 4 of 5 evaluable patients (80%) showed a peripheral neuropathy. The cumulative dose at the first signs of peripheral neuropathy was between 425 to 880mg.

The analysis of the pooled data of the systemic literature review showed an objective overall response rate of 74.2%. There was no publication of a dose finding study in CD30+ cutaneous lymphoma treated with brentuximab vedotin. An alternative therapeutic scheme has not been published either.

CONCLUSIONS: Brentuximab vedotin seems to be a powerful treatment option in refractory CD30+ cutaneous T-cell lymphoma. But there is no scientifically sound basis for the use of a therapeutic scheme of 1.8mg/kg every 3 weeks. In fact there is a trend that a dose reduction as well as prolonged treatment intervals works without any loss of response and with fewer side effects.

N-13 PEMBROLIZUMAB INDUCES A COMPLETE SKIN AND BLOOD RESPONSE IN A PATIENT WITH SYNCHRONOUS SEZARY SYNDROME AND METASTATIC MELANOMA

POSTER Lansigan F*, Yerrabothala S, Stearns D, Leblanc R, Gehr G, Shirai K, Zug K Dartmouth-Hitchcock Medical Center; Norris Cotton Cancer Center; Lebanon, New Hampshire, USA

Pembrolizumab is a humanized monoclonal immunoglobulin IgG4 antibody directed against human cell surface receptor PD-1 (programmed death-1) which is approved for the treatment of metastatic melanoma. We report a patient with Sezary syndrome who achieved a complete remission while being treated for a synchronous metastatic melanoma with pembrolizumab. An 86-year-old male with a history of polymyalgia rheumatica treated with a prednisone taper developed an erythematous, pruritic rash on the truck, groin and extremities. The skin biopsy was consistent with cutaneous T-cell lymphoma. Peripheral blood flow cytometry revealed CD4+/CD7- (922cells/mcl) and CD4+/CD26- (978cells/mcl) Sezary cells. A CT scan revealed a left upper lung 24x26x34 mm mass and left axillary adenopathy. A lung biopsy unexpectedly revealed metastatic melanoma, BRAF unmutated, and further history revealed a prior resected melanoma of his left cheek 18 years prior. He was diagnosed with synchronous Stage IIA(B1) CTCL and metastatic melanoma. The patient was started on extracorporeal photopheresis (ECP) two consecutive days every four weeks with improvement of the rash and pruritus. Melanoma was treated with ipilumumab 3mg/kg every 2 weeks for 4 cycles while ECP continued. The melanoma responded but the CTCL progressed to erythroderma and B2 disease. Bexarotene was added to ECP with little effect. Six months later, repeat PET showed melanoma progression and pembrolizumab 2 mg/kg was started every 3 weeks. Remarkably, the erythroderma improved within 2 weeks; after 3 cycles of pembrolizumab, the erythroderma resolved completely. Peripheral blood flow cytometry after 4 cycles revealed no abnormal circulating T-cells. A skin biopsy of a small remaining patch revealed a decrease in CD4-positive T-cells and an increase in CD8-positive T-cells compared to previous biopsies. Blocking the PD1 and PD-L1 pathways may be important in some patients with CTCL/SS. Phase II clinical trials are ongoing to investigate the use of pembrolizumab in the treatment of MF/SS. The complete response in skin and blood in this patient to pembrolizumab is remarkable. Further understanding of the clinical and molecular determinants of responders will be important in identifying subsets of patients most likely to benefit from this new targeted therapy.

N-14 TOTAL SKIN ELECTRON BEAM THERAPY AS MAINTENANCE SKIN-DIRECTED THERAPY IN SEZARY SYNDROME

POSTER Spicknall KE*, Breneman D, Breneman JC University of Cincinnati, Cincinnati OH USA

INTRODUCTION: Total skin electron beam therapy (TSEBT) is highly effective in the treatment of cutaneous T-cell lymphoma, however relapse occurs in most patients. We explored the use of weekly maintenance palliative TSEBT fractions for the treatment of disabling generalized pruritus in a patient with Sezary syndrome.

METHODS: A 67-year-old man presented with a two year history of severe generalized pruritus, rash and recent onset of weakness and weight loss. Skin biopsy of the back revealed epidermotropism of CD3+, CD4+ and CD8- lymphocytes, as well as a superficial perivascular infiltrate of identical lymphocytes. Bone marrow biopsy with flow cytometry revealed infiltration by a similar abnormal population of T cells which were CD3+, CD4+, CD7-, and CD8-; these findings were initially interpreted as prolymphocytic leukemia with cutaneous involvement and the patient was treated with multi-agent chemotherapy and alemtuzumab with complete response in the bone marrow but persistent pruritus and rash. Skin examination at that time revealed pink to tan, slightly scaling, reticulated patches involving the trunk and extremities; severe pruritus affected clinically normal-appearing skin. The patient was treated with low dose TSEBT (total dose 10.8Gy) with resolution of pruritus and rash. RESULTS: Because of quick recurrence of generalized pruritus following TSEBT and the short survival expected in prolymphocytic leukemia, weekly maintenance TSEBT treatments were administered for a total of 52 weeks, in combination with psoralen plus UVA twice to three times weekly with excellent control of pruritus. Maintenance dosing started at 100cGy and was tapered to 60cGy; doses below 60cGy resulted in recurrent pruritus. Eight months following discontinuation of TSEBT severe pruritus recurred and the bone marrow revealed relapsed leukemia. The patient passed away from sepsis more than three years after his leukemia diagnosis. Taking together the patient's generalized pruritus, histologic and immunohistochemical findings in the skin and bone marrow, and longer than expected survival for prolymphocytic leukemia, we believe his presentation was most consistent with Sezary syndrome.

CONCLUSIONS: Weekly maintenance TSEBT may be an effective palliative treatment for some patients with disabling pruritus of Sezary syndrome.

Abstracts * indicates presenting author

Scientific Session O. Therapeutics 3: Endpoints & Clinical Trials

O-01 EXPLORING NEW MEANINGFUL ENDPOINTS FOR CTCL CLINICAL TRIALS IN TWO PHASE II STUDIES OF BRENTUX-IMAB VEDOTIN (BV) IN PATIENTS WITH MYCOSIS FUNGOIDES (MF) AND SÉZARY SYNDROME (SS)

ORAL Kim YH*1, Horwitz SM², Talpur R³, Rahbar Z¹, Li S¹, and Duvic M³

¹Stanford Cancer Institute, Stanford, CA; ²Memorial Sloan Kettering Cancer Center, New York, NY; ³MD Anderson Cancer Center, Houston, TX

INTRODUCTION: CTCL has unique symptoms, including disturbing visible and pruritic qualities that impact treatment decisions, complicating traditional trial endpoints, including overall response rate (ORR), progression-free survival (PFS), and duration of response (DOR). Objective responses with >50% reduction may not equal clinical benefit, and symptomatic patients may receive new therapy without objective progression, censoring them for PFS and DOR. Meaningful impact of CTCL therapy should reflect ORR and DOR unaffected by new treatment. Moreover, complete clearing (CR) of the skin, which may provide added clinical benefit, is infrequently observed with systemic therapy alone. We explored new endpoints combining ORR and DOR and highlight near CR+CR in pooled data from the two phase II BV trials.

METHODS: We defined ORR4 and ORR6 as objective responses lasting at least 4 and 6 months, respectively, without initiation of new therapy. Those with >90% reduction in mSWAT (near CR+CR) were designated as CR90. Two trials had similar eligibility, treatments, and assessments.

RESULTS: 71 pts (MDACC 38, Stanford 33) were included in the pooled analyses with median age, 65; 94% MF; 14 (20%) stage IB/ IIA, 57 (80%) advanced stage (34 IIB, 22 IV); 52% LCT, 44% F-MF; median prior systemic treatments 3. ORR was 62% (44/71) with CR90 of 24% (17/71). At 6 and 12 months, KM estimates showed 79% and 53% of responses continuing and 76% and 53% progression-free, respectively; however, subjects censored for starting a new significant therapy without objective progression were 17/44 and 30/71 for DOR and PFS calculations, respectively. ORR4 was 51% (36/71) and ORR6, 34% (24/71). Those with CR90 had significantly higher ORR4 and ORR6 than those without CR90, p <.0001 and p=.0007, respectively.

CONCLUSIONS: We suggest ORR4 or ORR6 that capture response rate and duration as a single endpoint as an alternative or additional measure of clinical efficacy of systemic therapies in MF/SS. Evaluating the CR90s may identify a subset with greater clinical benefit from systemic therapies undergoing clinical development.

O-02 KIR3DL2 EXPRESSION IN CUTANEOUS T-CELL LYMPHOMAS: A WIDELY-SHARED TARGET

ORAL Battistella M¹*, Leboeuf C¹, Ram-Wolff C², Bonnafous C³, Sicard H³, Janin A¹, Bagot M²

¹Pathology Department, INSERM U1165, Université Paris 7, AP-HP Hôpital Saint Iouis, France; ²Dermatology Department, INSERM U976, Université Paris 7, AP-HP hôpital Saint Louis, France; ³Innate Pharma, Marseille-Luminy, France.

INTRODUCTION: KIR3DL2, a killer immunoglobulin-like receptor normally expressed by minor subsets of CD8+ T cells and natural killer (NK) cells is aberrantly expressed in circulating and skin Sézary cells, in some transformed mycosis fungoides (tMF), and has more recently been found in primary cutaneous anaplastic large cell lymphoma (pcALCL). As KIR3DL2 appears a promising target for CTCL therapy, we aimed to study its expression in a large series of CTCL, including all WHO subtypes.

METHODS: 152 frozen biopsy samples from 131 CTCL patients, 11 Erythrodermic Inflammatory Disease (EID) patients, and 10 healthy patients were available for KIR3DL2 evaluation using immunohistochemistry on frozen section with the novel KIR3DL2-specific 12B11 monoclonal antibody.

KIR3DL2 expression was assessed blindly by 2 pathologists, counting the percentage of positive cells in the mononucleated skin infiltrate in 10 high-power fields. The median percentage of KIR3DL2+ cells was analysed in all CTCL subsets, compared with EID or healthy skin. KIR3DL2 expression was also compared to pathological features, and to ISCL-EORTC stage of the disease

RESULTS: A median of 0.2% (0-1.3) KIR3DL2+ cells was found in healthy skin samples, and 4.85% (0.5-8.5) in EID skin samples. In CTCL patients, 86/131 samples (65.6%) had > 5% KIR3DL2+ cells, in all CTCL subtypes. Especially, KIR3DL2 was diffusely expressed in SS (median of 62.5% KIR3DL2+ cells; n=21), pcALCL (66.75% of cells; n=11), gamma-delta T-cell lymphoma (75% of cells; n=3), and CD8+ aggressive epidermotropic lymphoma (45.5% of cells; n=2). Considering 5% KIR3DL2+ cells as a threshold, KIR3DL2 expression was also found in MF (conventional, adnexotropic, granulomatous; 40/73 samples), panniculitis-like subcutaneous T-cell lymphoma (1/1), HTLV1+ lymphoma (3/4), PTCLnos (3/6), lymphomatoid papulosis (2/6) and T/NK nasal-type lymphoma (2/4).

Regarding all MF/SS patients (n=94), KIR3DL2 expression increased with ISCL-EORTC stage (p=0.0004; Kruskal-Wallis test). Largecell transformation was clearly associated with more pronounced KIR3DL2 expression, whatever the stage (median 3.55% KIR3DL2+ cells in MF vs 60% in tMF, p=0.0003; Mann-Whitney U test).

CONCLUSIONS: A majority of CTCL (65.6%) express KIR3DL2, with SS, tMF, pcALCL, gamma-delta T-cell lymphoma and CD8+ aggressive epidermotropic lymphoma showing the most significant expression. In MF/SS patients, KIR3DL2 expression increases together with ISCL-EORTC stage, and is more pronounced in SS and tMF than in conventional, granulomatous or adnexotropic MF. This study indicates that patients with KIR3DL2 expression may be found among all subtypes of CTCL, and may be candidate for KIR3DL2-targeted therapy.

Scientific Session O. Therapeutics 3: Endpoints & Clinical Trials

O-03 FIRST-IN-HUMAN, OPEN LABEL, MULTICENTER PHASE I STUDY OF IPH4102, FIRST-IN-CLASS HUMANIZED AN-TI-KIR3DL2 MONOCLONAL ANTIBODY, IN RELAPSED/REFRACTORY CUTANEOUS T-CELL LYMPHOMAS: PRELIMINARY SAFETY AND CLINICAL ACTIVITY RESULTS

ORAL Bagot M^{*1,7}, Porcu P³, Ram-Wolff C^{1,7}, Vermeer M⁴, Khodadoust M², Duvic M⁵, Whittaker S⁶, Mathieu S¹, Battistella M¹, Marie-Cardine A^{1,7}, Bensussan A^{1,7}, Sicard H⁸, Paiva C⁸, Pilz K⁸, Kim YH²

¹Hôpital Saint Louis – 1 Avenue Claude Vellefaux, 75475 Paris cedex 10, France; ²Stanford Cancer Institute - Palo Alto, CA 94304, USA; ³Ohio State University – Columbus, OH, USA; ⁴LUMC - Leiden, the Netherlands; ⁵MD Anderson Cancer Center – Houston, TX, USA; ⁶Guy's and St Thomas' Hospital – London, UK; ⁷INSERM U976, Hôpital St Louis, 75475 Paris Cedex 10, France; ⁸INNATE PHARMA, 117 Avenue de Luminy, 13009 Marseilles, France

INTRODUCTION: KIR3DL2 is expressed in all subtypes of Cutaneous T-cell Lymphomas (CTCL), irrespectively of disease stage, with the highest prevalence of expression in Sézary Syndrome (SS) and transformed Mycosis Fungoides (MF), two subsets with high unmet need. KIR3DL2 belongs to the killer immunoglobulin-like receptor (KIRs) family expressed on minor populations of NK, CD8 and CD4 T cells. IPH4102 is a first-in-class anti-KIR3DL2 monoclonal antibody (mAb). It selectively depletes KIR3DL2-expressing cells. IPH4102 has shown potent efficacy in preclinical models, in particular ex vivo autologous assays using primary CTCL cells. IPH4102 effects in CTCL patients are currently evaluated in a Phase I study.

METHODS: IPH4102-101 (NCT02593045) is a first-in-Human phase I dose-finding study evaluating repeated administrations of single-agent IPH4102 in relapsed/refractory CTCL patients. The primary objective of the study is to assess the safety and tolerability of increasing doses of IPH4102 by characterizing dose-limiting toxicity and adverse events. The study has two sequential portions, a dose-escalation followed by cohort expansion portion. The dose-escalation portion has a 3+3 design with accelerated titration and aims to determine the maximal tolerated dose (MTD) or recommended Phase 2 dose (RP2D). Secondary objectives include PK, immunogenicity and signals of anti-neoplastic clinical activity. Eligible CTCL patients must have received at least 2 lines of systemic therapy. Centrally assessed KIR3DL2 expression on malignant cells in skin or blood is required. In the expansion portion, two CTCL subtype-specific cohorts will each include 10 additional patients to further explore the MTD or RP2D.

RESULTS: Enrollment into study IPH4102-101 started in November 2015. Dose levels 1-5 have been completed without DLT, with a total of 9 patients treated and evaluable for safety and clinical activity assessments. These comprise 6 SS, 2 MF and 1 "Not Otherwise Specified" CD4⁺ CTCL patients. Overall, only few low grade related adverse events have been reported with IPH4102 treatment. Preliminary safety and clinical activity results observed in patients treated up to dose-level #5 will be presented.

CONCLUSIONS: Preliminary data from phase 1 study of novel targeted immune therapy show excellent tolerability in advanced CTCL patients and the study continues to enroll.

O-04 E7777 DEMONSTRATED SAFETY IN PERSISTENT OR RECURRENT CUTANEOUS T-CELL LYMPHOMA

ORAL Duvic M*¹, Kuzel TM², Dang NH³, Prince HM⁴, Feldman T⁵, Foss FM⁶, Ren M⁷, Mody K, Ooi C,⁷ Reyderman L⁷, Kim YH⁸ ¹Department of Dermatology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²Division of Hematology/ Oncology/Cell Therapy, Rush University Medical School, Chicago, IL, USA; ³Division of Hematology and Oncology, University of Florida, Gainesville, FL, USA; ⁴Department of Haematology, Peter MacCallum Cancer Centre, Melbourne, Australia; ⁵Lymphoma Division, The John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ, USA; ⁶Yale Cancer Center, Yale Medical Group, New Haven, CT, USA; ⁷Esiai Inc., Woodcliff Lake, NJ, USA; ⁸Stanford Cancer Center, Stanford University, Stanford, CA, USA

INTRODUCTION: E7777 is a recombinant cytotoxic fusion protein composed of diphtheria toxin fragments A and B and human interleukin-2. Its amino acid sequence is identical to denileukin diffitox (DD; approved in the United States (US) for treatment of persistent or recurrent cutaneous T-cell lymphoma [CTCL]) but purity and concentration of active protein monomer species is improved. This is a multicenter, open-label, single-arm study with a lead-in phase to select the E7777 dose for the main study in which efficacy and safety will be assessed.

METHODS: A Continual Reassessment Method was used, with dose designed to target a dose-limiting toxicity (DLT) rate of ~20%. Key inclusion criteria included patients aged \geq 18 years, with diagnosis of Mycosis Fungoides (MF) or Sézary Syndrome (SS), who had a measurable CD25+ tumor, and received \geq 1 prior CTCL therapy. Prior commercial DD therapy was not allowed. Patients received E7777 from 6 to 15 µg/kg intravenously on 5 consecutive days in 21 day cycles.

RESULTS: Twenty-one patients were enrolled in the lead-in phase; 16 with MF (Stage IV disease=7) and 5 with SS (Stage IV). Patients were treated for a median of 6 (range: 1–21) cycles. Of patients who discontinued the study, eleven were due to disease progression, five due to adverse events (AEs), and two due to patient/physician choice. There were no treatment-related deaths during the study. Two DLTs of capillary leak syndrome (CLS) occurred at 15 µg/kg. Serious AEs considered related to treatment were CLS (n=2, 15µg/kg); vomiting (n=2, 12µg/kg); acute kidney injury, deep vein thrombosis, hypoalbuminemia, pulmonary embolism, thrombocytopenia, diarrhea, tumor flare, and nausea (n=1 each, 12µg/kg); and pruritus and rash (n=1 each, 9µg/kg). The selected main study dose was 9 µg/kg, based on lead-in maximum tolerated dose and safety data and results from a parallel phase 1 study in Japan. Pharmacokinetic and immunogenicity analyses will be presented.Emphasise new and important aspects of the study and conclusions that are drawn from them.

CONCLUSIONS: The safety profile of E7777 was similar to denileukin diftitox. The main study, now opened at six US and one Australian site, has a planned enrollment of 70 patients receiving E7777 at 9 µg/kg.

Scientific Session O. Therapeutics 3: Endpoints & Clinical Trials

O-05 A SINGLE-ARM PHASE 2A STUDY OF NM-IL-12 (rHu-IL12) IN PATIENTS WITH MYCOSIS FUNGOIDES-TYPE CTCL (MF) UNDERGOING LOW-DOSE TOTAL SKIN ELECTRON BEAM THERAPY (LD-TSEBT)

ORAL Kim YH¹, Hoppe RT^{*1}, Rook AH², Maity A², Buchanan M², Geskin LJ³, Horowitz D³, Finnegan G³, Patrone CC³, Khodadoust M¹, Lares A¹, Hong EK¹, Lawrence C⁴, Vainstein V⁴, Basile L⁴

¹ Stanford Cancer Institute, Depts of Dermatology and Radiation Oncology; ² Perelman School of Medicine, University of Pennsylvania, Depts of Dermatology and Radiation Oncology; ³ Cutaneous Oncology Center Columbia University, Depts of Dermatology and Radiation Oncology; ⁴ Neumedicines Inc.

INTRODUCTION: Multiple treatment modalities are available for MF, but most result in inevitable relapse. Therefore, new treatment strategies that improve response rate and prolong response duration are greatly needed. TSEBT is a highly effective therapy in MF. LD-TSEBT (12 Gy) is much more tolerable than the conventional 36+ Gy dose, thereby allowing for re-treatment; however, LD-TSEBT has a less favorable complete response rate and response duration. Combining LD-TSEBT with immunostimulatory modalities in MF has a strong biological rationale, since radiation-induced exposure of cancer-specific antigens should be synergistic with concomitant stimulation of anti-cancer immune responses. Interleukin-12 is a robust candidate for radioimmunotherapy as IL-12 has significant anti-MF activity as monotherapy, is very well tolerated without overlapping toxicity with TSEBT, and is a potent stimulator of innate and adaptive immunity.

METHODS: We report on a single-arm open-label phase 2a trial of combination of LD-TSEBT and NM-IL-12. Ten patients are planned for enrollment. Eligibility includes MF-type CTCL stages IB-IIIB and patients must be eligible for LD-TSEBT. TSEBT is started on study day 1 (fractionated 4 Gy/week, up to 12 Gy). NM-IL-12 is administered subcutaneously at 150 ng/kg on days 2 and 15, followed by 6 maintenance doses q4w at 100 ng/kg. The primary endpoint is safety with secondary endpoints being response rate and PFS.

RESULTS: Currently, 6 patients are enrolled, 5 evaluable for response; 4 male; median age 55; 3 stage IB, one IIB and one IIIB. Median number of previous therapies is 2 (0-6). The treatment was well-tolerated with only grade 1 or 2 AEs; most common AEs include chills and rash. One patient achieved CR, 2 PR, and 2 SD. Median follow-up is 15 weeks and 5 patients remain on study. One patient has been withdrawn from the study due to development of a suspected PLC-like skin reaction requiring topical steroid therapy.

CONCLUSIONS: These early results demonstrate that NM-IL-12 can be safely administered together with LD-TSEBT in CTCL patients. Encouraging clinical activity is observed including a CR. Enrollment is currently ongoing.

O-06 LENALIDOMIDE IN RELAPSED OR REFRACTORY PRIMARY CUTANEOUS LARGE B-CELL LYMPHOMAS, LEG-TYPE: FIRST RESULTS OF A MULTICENTRIC PROSPECTIVE PHASE II TRIAL "REV-LEG"

ORAL Beylot-Barry M*^{1,2,3}, Mermin D², Bouabdallah R⁴, Bonnet N^{3,5}, Duval-Modeste AB^{3,6}, Mortier L^{3,7}, Oro S^{3,8}, Ram-Wolff C^{3,9}, Barete S^{3,10}, Dalle S^{3,11}, Maubec E^{3,12}, Quereux G^{3,13}, Templier I^{3,14}, Bagot M^{3,9}, Grange F^{3,15}, Joly P^{3,6}, Vergier B^{1,3,16}, Pham-Ledard A^{1,2}, Doussau A¹⁷, Maillard A¹⁷, Merlio JP^{1,3,18}, and the-French Study Group on cutaneous lymphomas (GFELC)

¹INSERM U1053,Bordeaux research in Translational Oncology, Team 3 oncogenesis of cutaneous lymphomas, Univ. Bordeaux, France; ²Dermatology Department, CHU Bordeaux, Bordeaux, France; ³French Study Group for Cutaneous Lymphomas, France (GFELC); ⁴Cancer Canter Institute, Marseille, France; ⁵Department of Dermatology, CHU Marseille, Marseille, France; ⁶Dermatology Department, CHU Rouen, Rouen, France; ⁷Dermatology Department, CHU Lille, Lille, France; ⁸Dermatology Department, University Hospital Henri Mondor, Créteil, France; ⁹Dermatology Department, University Hospital Saint-Louis, Paris, France; ¹⁰Dermatology Department, University Hospital Tenon, Paris, France; ¹¹Dermatology Department, CHU Lyon, Lyon, France; ¹²Dermatology Department, University Hospital Bichat, Paris, France; ¹³Dermatology Department, CHU Nantes, Nantes, France; ¹⁴Dermatology Department, CHU Grenoble, Grenoble, France; ¹⁵Dermatology Department, CHU Reims, Reims, France; ¹⁶Pathology Department, CHU Bordeaux, Pessac, France; ¹⁷Clinical Epidemiology Unit, CHU Bordeaux, Bordeaux, France; ¹⁸Tumor Bank and Tumor Biology Laboratory, CHU Bordeaux, Pessac, France.

INTRODUCTION: Prognosis of primary cutaneous large B-cell lymphoma leg type (PCBCL-LT) is improved by first-line treatment with rituximab-polychemotherapy (R-PCT). However, the advanced age of patient limits therapeutic options in relapsing or refractory cases.

METHODS: A multicenter single arm phase II trial was conducted in the GFELC to assess benefit of lenalidomide in refractory or relapsing PCBCL-LT after R-PCT. Lenalidomide: 25 mg/d for 21 days; 28 days cycle; 12 cycles unless progression. Primary endpoint: overall response (complete response CR, partial response PR) at 6 months. Secondary endpoints: overall survival, progression-free survival (PFS), tolerance, identification of prognostic factors. Study designed (Simon scheme) in two phases with an interim analysis (minimum acceptable effectiveness threshold: 20% CR/PR). Due to a lower recruitment than expected (19 vs 37) the trial was interrupted after 32 months before results of interim analysis.

RESULTS: 19 patients (median age 79 years, 16 women) were enrolled between July 2012 and September 2014. Median time from R-PCT was 1 year. Stages were T1 (n=2), T2 (n=13), T3 (n=4). The median number of lenalidomide cycles was 6. The 6 months response rate was 26.3% (11-47.6%, IC90%) including 4 CR and 1 PR. At 12 months, there were still 2 CR and 1 PR. Median PFS was 5 months. Overall survival probabilities at 6 and 12 months were 89.5% (64.1-97.3, IC:95%) and 68.4% (42.8-84.4%, IC:95%). At the end point date, 11 patients died, 9 due to lymphoma, Grade 3 adverse events (AE) were mainly neutropenia and thrombocytopenia. Two deaths were due to AE: sepsis complicating neutropenia and thromboembolic event. Factors associated with response are now being analysed.

Scientific Session O. Therapeutics 3: Endpoints & Clinical Trials

CONCLUSIONS: Our results, while limited by lack of power, suggest a modest response rate with lenalidomide that does not justify its use as first line. Severe AE were observed and others have justified dose reduction. However, a prolonged CR was obtained in some patients. Response markers are needed to stratify the use of lenalidomide in second line, possibly at a reduced dose and therapeutic associations have to be investigated.

O-07 PHASE 1, SINGLE-ARM, OPEN-LABEL, DOSE ESCALATION TRIAL OF MICRONEEDLE ARRAY-DOXORUBICIN IN PA-TIENTS WITH CUTANEOUS T CELL LYMPHOMA

ORAL Akilov O*, McCann S, Erdos G, Falo LD Jr. Department of Dermatology, University of Pittsburgh, Pittsburgh, PA

INTRODUCTION: Ultra-low doses of the chemotherapeutic agent, doxorubicin, could be delivered directly into the microenvironment of malignant cells with microneedle array (MNA). We hypothesize that such in situ, chemo-immunization will result in tumor destruction and the induction of potent, immunogenic anti-tumor responses. The primary objective is to establish a safe dose of

doxorubicin when delivered via the MNA system. METHODS: This initial Phase 1 clinical trial incorporates a single-arm, placebo-controlled (within patient), open-label, traditional 3+3 dose escalation study design to determine the Maximum Tolerated Dose (or Effective Dose) of doxorubicin; followed by an extended evaluation of safety and effectiveness at the determined Maximum Tolerated Dose (or Effective Dose).

RESULTS: An initial cohort of 3 patients received one cycle of MNA-D (applied to 3 lesions) at a 25 μ g doxorubicin dose and MNA placebo (applied to 1 lesion; to control for the possibility that the MNA, itself, may induce direct skin irritation). A cycle was five weeks in duration with MNA-D administered once weekly for the first four weeks followed by one week of no treatment; the latter permitting an evaluation of potential delayed adverse effects. No delayed limited toxicities or > Grade 3 unrelated adverse events were observed, and the dose of MNA-D was escalated to 50 μ g, and a new cohort of 3 patients was freated in the same fashion.

CONCLUSIONS: We will present the ongoing results of this trial and discuss potential development of a novel chemo-immunization strategy which augments tumor antigen presentation in situ.

O-08 INTERIM ANALYSIS OF PHASE II CLINICAL TRIAL PIMTOMF (TOPICAL PIMECROLIMUS IN EARLY MF) EUDRA CT 2014-001377-14

ORAL Ortiz-Romero PL^{*1}, Maroñas-Jiménez L¹, Muniesa C³, Estrach T², Servitje O³, Fernández de Misa R⁴, San Martín O⁵, Gallardo F⁶, Combalía A², Riveiro-Falkenbach E¹, Postigo C¹, Vega R¹, Gómez de la Cámara A¹, Rodríguez Peralto JL¹, Vaqué JP⁸, Alonso R⁸, Sánchez-Beato M⁷, Piris MA⁸

¹Hospital Universitario 12 de Octubre, Instituto de Investigación i+12. Madrid. ²Hospital Clinic de Barcelona. Universitat de Barcelona .Idibaps ³Hospital Universitari de Bellvitge, Barcelona. ⁴Hospital Nuestra Señora de la Candelaria. Santa Cruz de Tenerife. ⁵IVO, Valencia. ⁶Hospital del Mar. Barcelona. ⁷Instituto de Investigación Sanitaria Puerta de Hierro-Majadahonda. Madrid. ⁸UC-IBBTEC, IDIVAL. Santander

INTRODUCTION: Several groups have found activating mutations in PLCG1affecting a range of 5-20% of the MF cases studied. Mechanistically, Calcineurine (CaN) is a well-known downstream effector of PLCG1 activity. Interestingly, this pathway is activated in MF with a frequency higher than PLCG1 mutations. To test the efficacy and safety of treatment MF patients with CaNinhibitors, we organized a phase II clinical trial

METHODS: Study population: MF, stages Ia, Ib, IIa. Statistical considerations recommended a population size of 40 patients. Treatment: Topical pimecrolimus (10 mg/g)/12h for a maximum of 16 weeks with posterior follow up of 12 months. Study Objective: Primary: Response rate. Secondary: Duration of response, disease free survival, progression free survival, safety, second tumours, translational research. Biopsies for translational research were taken pre and post treatment.

RESULTS: Until May30th, 2016, 39 patients have been included in the trial. Mean age was 51.6 y.o (range: 20-81); M/F: 24/15; Stages: Ia (26 pat), Ib (13 pat); Mean basal mSWAT was 14.5 (range: 1-79). 37 patients have completed 16 weeks of treatment. One of them progressed. Response rate was 54% (1CR, 19 PR). 16 patients showed stable disease. No grade III or higher adverse events appeared. No second tumors or tumoral progression of MF appeared.

Until now, half of the samples have been analyzed by targeted sequencing as well as IHC biomarkers. Mutational status and mechanistic changes changes during the evolution of the disease are currently under analysis. Emphasise new and important aspects of the study and conclusions that are drawn from them.

CONCLUSIONS: Topical pimecrolimus is active and safe in early mycosis fungoides.

Scientific Session O. Therapeutics 3: Endpoints & Clinical Trials

0-09 A FIRST IN HUMAN EXPERIENCE OF THE ANTI-CD37 ANTIBODY-DRUG CONJUGATE AGS67E IN LYMPHOID MALIGNANCIES, WITH EXCITING EARLY ACTIVITY IN CTCL

ORAL Sawas A*, Savage KJ, Perez RP, Advani RH, Melhem-Bertrandt A, Lackey J, Trave F, Anand B, Huang Y, Vincent M, Reyno LM, O'Connor OA Columbia University Medical Center, New York, NY; British Columbia Cancer Agency Center for Lymphoid Cancer, Vancouver, BC, Canada; University of Kansas, Fairway, KS; Stanford University School of Medicine, Stanford, CA; Astellas Pharma Global Development, Northbrook, IL; Agensys, Inc, Santa Monica, CA; Agensys Inc, Santa Monica, CA

INTRODUCTION: CD37 is a tetraspanin expressed in most B- and T- cell malignancies in previous tumor profiling studies (Pereira et al, Mol Cancer Ther; 2015). AGS67E, is an antibody drug conjugate (ADC) composed of a fully human IgG2 antibody targeting CD37 that is conjugated to the microtubule-disrupting agent MMAE through a cleavable linker. CD37 expression is found in: > 80% of B and T-cell lymphomas as well as in 100% of Chronic lymphocytic leukemia (CLL) samples tested. CTCL is a disease that is usually under represented in phase I clinical trials.

METHODS: The first in human, ongoing, multicenter, phase 1 dose-escalation study is currently evaluating the safety, PK and anticancer activity of AGS67E given as monotherapy to subjects with relapsed / refractory NHLs and CLL. AGS67E is administered IV Q3 weeks until disease progression or unacceptable toxicity. The dose escalation will first determine the maximum tolerated dose (MTD) without growth factor (GF), followed by the MTD with GF support.

Type of lymphoid malignancy	Ν	(%)
Non-Hodgkin Lymphoma B-Cell	34	(71%)
Non-Hodgkin Lymphoma T-Cell	14	(29%)
Total	48	
Type of NHL		
BURKITT'S LYMPHOMA "LEUKEMIA VARIANT"	1	(2%)
CUTANEOUS MARGINAL ZONE LYMPHOMA/LOW-GRADE B-CELL	1	(2%)
Follicular Lymphoma(FL)	7	(15%)
MALT(MALT)	1	(2%)
Mantle Cell Lymphoma(MCL)	2	(4%)
Diffuse Large B-Cell Lymphoma(PDLBCL)	17	(35%)
Small Lymphocytic LYMPHOMA(CLL/SLL)	1	(2%)
Transformed Diffuse Large B-Cell Lymphoma(TDLBCL)	3	(6%)
WALDENSTROM MACROGLOBULINEMIA(WM)	1	(2%)
ADULT T-CELL LEUKEMIA	3	(6%)
PERIPHERAL T-CELL LYMPHOMA(PTCL)	3	(6%)
MYCOSIS FUNGOIDES(MF)	4	(8%)
EATL(EATL)	1	(2%)
T-CELL LYMPHOBLASTIC LYMPHOMA(T-LBL)	1	(2%)
T-cell rich B-cell lymphoma (T/HRBCL)	1	(2%)
Prolymphocytic leukemia(PLL)	1	(2%)

RESULTS: As of August 8, 2016, 48 subjects have been treated of which 3 (6%) have a diagnosis of CTCL. Median age was 64 years (range 25 - 85). Subjects received a median number of 2 (1 - 11) prior therapies. The MTD was 0.9 mg/kg without GF; the dose limiting toxicity (DLT) was Gr 4 neutropenia 8 - 15 days after 1st dose. No major non-hematological toxicities have been observed. Eight subjects experienced symptoms of peripheral neuropathy: 5 (Gr 1) and 3 (Gr 2). The MTD with GF was 1.5 mg/kg. Responses were noted in subjects dosed at 0.9 , 1.2 and 1.5 mg/kg; Specifically, 6 subjects experienced a complete remission (CR) (4 Diffuse Large B-Cell Lymphoma (DLBCL), MALT and Follicular Lymphoma) and 3 subjects (Prolymphocytic leukemia (PLL), Mycosis Fungoides and DLBCL) experienced a partial remission (PR). The serum AGS67E concentrations indicated a non-linear PK at \leq 0.6 mg/kg dose levels. At 1.2 mg/kg, the half-life of AGS67E and free MMAE ranged from 1.59-2.25 and 2.34-3.64 days, respectively.

CONCLUSIONS: AGS67E has a favorable safety profile and has demonstrated signs of activity, especially in CTCL. Expansion cohorts are ongoing at the MTD with GF for DLBCL and T-Cell lymphoma. Clinical trial information: NCT02175433

Scientific Session O. Therapeutics 3: Endpoints & Clinical Trials

O-10 PEMBROLIZUMAB FOR TREATMENT OF RELAPSED/REFRACTORY MYCOSIS FUNGOIDES AND SÉZARY SYNDROME: CLINICAL EFFICACY IN A CITN MULTICENTER PHASE 2 STUDY

ORAL Khodadoust MS^{*1}, Rook AH², Porcu P³, Foss F⁴, Moskowitz A⁵, Shustov AR⁶, Shanbhag S⁷, Sokol L⁸, Shine R⁹, Fling SP⁹, Li S¹, Rahbar Z¹, Kim J¹, Yang Y⁹, Yearley J¹⁰, Chartash EK¹⁰, Townson SM¹⁰, Subrahmanyam PB¹, Maecker H¹, Alizadeh AA¹, Dai J¹, Horwitz SM⁵, Sharon E¹¹, Kohrt HE¹, Cheever MA^{6,9A}, Kim YH¹

¹Stanford University School of Medicine, Stanford, CA; ²University of Pennsylvania, Philadelphia, PA; ³The Ohio State University, Columbus, OH; ⁴Yale University School of Medicine, New Haven, CT; ⁵Memorial Sloan Kettering Cancer Center, New York, NY; ⁶University of Washington, Seattle, WA; ⁷Johns Hopkins University School of Medicine, Baltimore, MD; ⁸H Lee Moffitt Cancer Center, Tampa, FL; ⁹Fred Hutchinson Cancer Research Center, Seattle, WA; ¹⁰Merck Research Laboratories, Kenilworth, NJ; ¹¹Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, MD

INTRODUCTION: Malignant T-cells in mycosis fungoides (MF) and Sézary syndrome (SS) express PD-1 and have been found to harbor genomic rearrangements of PD-L1 and PD-L2. We explored the clinical activity of pembrolizumab, an immune checkpoint inhibitor of the PD-1/PD-L1 axis, in MF/SS.

METHODS: Twenty-four patients (pts) with MF/SS stages IB-IV treated with at least 1 prior systemic therapy were enrolled in this phase 2, single-arm study coordinated by the Cancer Immunotherapy Trials Network (CITN). Pembrolizumab was administered at 2 mg/kg every 3 weeks and treatment was allowed up to 2 years. The primary endpoint was overall response rate (ORR) as determined by the consensus global response criteria. Secondary endpoints were safety/tolerability, time to response (TTR), duration of response and progression-free survival (PFS).

RESULTS: Patients were advanced stage with 23 patients (96%) stage IIB or higher, including 15 pts (63%) with stage IVA SS. Most pts were heavily treated with a median of 4 prior systemic therapies. The median follow-up time was 40 weeks. ORR was 38% with 1 complete response and 8 partial responses. Six pts had 90% or greater improvement in skin disease as measured by mSWAT. The median TTR was 11 weeks. Responses were durable with 8 of 9 (89%) responses currently ongoing. An additional 9 pts (38%) had stable disease. The median PFS has not yet been reached, and the one-year PFS was 69%. There was no significant association between response and clinical characteristics including stage, disease type (MF vs. SS), and number of prior therapies, nor with skin tissue expression of PD-1, PD-L1, PD-L2, or infiltrating CD8+ T-cells. A skin flare reaction was seen in 40% of pts with SS, but treatment was otherwise well tolerated with a toxicity profile consistent with prior pembrolizumab studies. There were two treatment related serious adverse events: grade 2 pneumonitis and grade 3 diarrhea secondary to steroid-refractory duodenitis.

CONCLUSIONS: Pembrolizumab has significant clinical activity with durable responses seen in pts with previously treated MF/SS. A phase 2 trial of pembrolizumab in combination with interferon-gamma is being developed based on these results.

O-11 FIRST-IN-HUMAN, OPEN LABEL, MULTICENTER PHASE I STUDY OF IPH4102, FIRST-IN-CLASS HUMANIZED AN-TI-KIR3DL2 MONOCLONAL ANTIBODY, IN RELAPSED/REFRACTORY CUTANEOUS T-CELL LYMPHOMAS: PRELIMINARY RESULTS OF EXPLORATORY BIOMARKERS

POSTER Marie-Cardine A^{1,4}, Battistella M¹, Paturel C⁵, Bagot M^{1,4}, Kim YH², Porcu P³, Ram-Wolff C^{1,4}, Bonnafous C⁵, Khodadoust M², Thonnart N⁴, Widemann A⁵, Mathieu S¹, Bensussan A^{1,4}, Paiva C⁵, Pilz K⁵, Sicard H^{*5}

¹Hôpital Saint Louis, 1 Avenue Claude Vellefaux, 75475 Paris cedex 10, France; ²Stanford Cancer Institute - Palo Alto, CA 94304, USA; ³Ohio State University – Columbus, OH, USA; ⁴INSERM U976, Hôpital St Louis, 75475 Paris Cedex 10, France; ⁵INNATE PHAR-MA, 117 Avenue de Luminy, 13009 Marseilles, France

INTRODUCTION: KIR3DL2 is expressed in all subtypes of Cutaneous T-cell Lymphomas (CTCL), irrespective of clinical stage, with the highest prevalence of expression in Sézary Syndrome (SS) and large-cell transformed Mycosis Fungoides (MF), two subsets with high unmet need. KIR3DL2 belongs to the killer immunoglobulin-like receptor (KIRs) family expressed on minor populations of NK, CD8 and CD4 T cells. IPH4102 is a first-in-class anti-KIR3DL2 monoclonal antibody (mAb). It selectively depletes KIR3DL2-expressing cells. IPH4102 has shown potent efficacy in preclinical models, in particular ex vivo autologous assays using primary CTCL cells. Exploratory biomarkers of activity have been incorporated in the Phase I study of IPH4102 in CTCL patients.

METHODS: IPH4102-101 (NCT02593045) is a first-in-Human phase I study evaluating repeated administrations of single-agent IPH4102 in relapsed/refractory CTCL patients. The primary objective is to assess the safety and tolerability of increasing doses of IPH4102 by characterizing dose-limiting toxicity and adverse events. Secondary objectives include PK, immunogenicity and signals of anti-neoplastic clinical activity. Exploratory biomarkers aim to characterize KIR3DL2-expressing and non-expressing immune cells in involved organs and monitor them along IPH4102 treatment. They also include assessment of SS patient NK cell function *ex vivo* pre-dose. Measurement of molecular residual disease is also performed in skin, blood and lymph nodes (when applicable).

RESULTS: Enrollment into study IPH4102-101 started in November 2015. Preliminary exploratory biomarker assessment results of patients treated up to dose-level #5 (n = 9, including 6 SS, 2 MF and 1 "Not Otherwise Specified" CD4⁺ CTCL patients) will be presented in context of the preliminary clinical activity findings.

CONCLUSIONS: Preliminary data from phase 1 study of novel targeted immune therapy show excellent tolerability in advanced CTCL patients and the study continues to enroll.

Abstracts .

* indicates presenting author

Scientific Session P: Clinical Management & Challenging Cases

P-01 THE EFFECT OF PHOTOTHERAPY ON PROGRESSION TO TUMORS IN PATIENTS WITH PATCH-PLAQUE STAGE MY-COSIS FUNGOIDES

ORAL Hoot JW^{*1}, Kho T², Lamm V⁶, Ho J², Akilov O¹

¹Department of Dermatology, University of Pittsburgh, Pittsburgh, PA; ²University of Pittsburgh School of Medicine, Pittsburgh, PA

INTRODUCTION: Phototherapy has been a mainstay in the treatment of mycosis fungoides (MF). However, the recent findings of UV-induced p53 mutations in advanced stages of MF suggested the potential role of phototherapy in the progression of MF. The objective of this study was to evaluate the effect of prior phototherapy on the rate of progression to tumor stage MF.

MÉTHODS: Retrospective analysis of patients seen in Cutaneous Lymphoma clinic at the University of Pittsburgh from 1979 to 2016. Patients who were initially diagnosed with stage IA or IB MF and subsequently developed tumors were included in the study. Time to progression and overall survival were compared between those who received phototherapy prior to developing tumors and those who did not.

RESULTS: 333 patients with MF were identified. 72 out of 333 patients had tumors at some point during their disease. 40 out of 72 patients were initially diagnosed with stage IA or IB MF. 27 out of 40 patients received phototherapy prior to the development of tumors and 13 did not. Patients who received phototherapy took a median of 3.60 years, with an interquartile range of 2.38 to 4.90 years, to progress to stage IIB (calculated as the time from date of tissue diagnosis to date of first documented tumor). Patients who did not receive phototherapy took a median of 1.56 years, with an interquartile range of 0.57 to 3.36 years, to progress to stage IIB. We found that the rate of progression to tumor stage was 2.37 (95% CI 1.86-2.89, p = 0.0016) times higher in patients who did not receive phototherapy.

CONCLUSIONS: The therapeutic effects of phototherapy appear to outweigh any of its potential adverse effects on the progression from patch-plaque to tumor stage MF.

P-02 TOTAL SKIN ELECTRON BEAM (TSEB) THERAPY FOR THE MANAGEMENT OF T CELL CUTANEOUS LYMPHOMAS. THE EVOLVING ROLE OF LOW DOSE (12 GY) TREATMENT SCHEDULE

ORAL Gerorgakopoulos J*1, Papadavid E¹, Platoni K¹, Dilvoi M¹, Patatoukas G¹, Nikolaou V², Antoniou C², Rigopoulos D¹, Kouloulias V¹ ¹Attikon University Hospital, Athens, Greece; ²A. Syggros Hospital, Athens, Greece

INTRODUCTION: Although rare, cutaneous lymphomas represent a separate entity in hematologic oncology. Cutaneous T cell lymphomas (CTCL) are most common, with Mycosis Fungoides (MF) accounting for about 50 to 70% of cases. Sezary Syndrome (SS), which represents the leukemic varian of MF, accounts for 3% of CTCL. Radiation therapy plays an integral part in the management of CTCL and especially MF. Treatment with electrons or photons and more specifically therapy via Total Skin Electron Beam Therapy (TSEB) is one of the many different skin directed treatment options. The scope of this study is to evaluate the effectiveness and toxicity of two treatment schedules of TSEB: the standard scheme of 36 Gy and the low dose scheme of 12 Gy.

METHODS: We publish our experience with TSEB in the management of MF and SS. 14 patients treated in our institution from 2011 to 2015. 8 patients received the 12 Gy (low dose) scheme and 6 patients were managed with 36 Gy (standard or full dose scheme) according to six dual field Stanford technique. We analyze overall response rate, duration of response and toxicity of treatment.

RESULTS: After a median follow up of 2,5 years we demonstrate excellent results, with both schemes being well tolerated and resulting in comparable response rates. The overall response rate for both treatment regimens was over 87,5%. Treatment was well tolerated with mild toxicity.

CONCLUSIONS: The role of TSEB in the management of MF and SS is well established. The low dose TSEB schedule of 12 Gy is an effective treatment option, since therapeutic results are more than acceptable, compliance is excellent and toxicity is minimal. The fact that it can be repeated safely in the course of a "regressive" disease makes it more attractive than the standard 36 Gy scheme when a patient is referred to radiation treatment according to treatment guidelines.

P-03 EYELID INVOLVEMENT BY MF/CTCL: A MANAGEMENT CHALLENGE

ORAL Kim EJ*1 | 1Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania

Mycosis fungoides subtype of cutaneous T-cell lymphoma (MF/CTCL) typically favors sun-protected areas. Patients who undergo skin directed therapies may develop skin lesions in sanctuary sites (eyelids, body folds, genitals, palms/soles). Eyelid involvement (ectropion) is observed in Sézary Syndrome but the prevalence of eyelid involvement in other stages of MF/CTCL is not known. Eyelid involvement by MF/CTCL is often symptomatic and is a challenge to treat with skin directed therapies due to potential irritation or eye toxicity. Case series of Stage IA – IIIB MF patients from 2011-2016 seen by a single provider (E.Kim), academic dermatology center. Sézary Syndrome patients were excluded. Over a 5 year period, out of 345 Stage IA – IIIB MF patients seen in clinic, 23/345 (6.6%) demonstrated eyelid involvement. 12/23 (52%) patients had early stage (Stage IA-IIIA), 11/23 (48%) had advanced stage disease (Stage IIB-IIIB). 8/23 (35%) had a history of folliculotropic disease. 5/23 (22%) were managed with skin directed therapies alone, 18/23 (78%) required addition of systemic therapy to manage their disease. Eyelid involvement in MF/CTCL is common, can be seen even in early stage disease. While selected skin directed therapies can be used judiciously, patients may require systemic agents to treat this "sanctuary site."

Scientific Session P: Clinical Management & Challenging Cases

P-04 THE FRENCH EXPERIENCE OF TREATMENT OF CUTANEOUS T CELL LYMPHOMA WITH BRENTUXIMAB VEDOTIN: A SERIES OF 32 CASES.

ORAL Mathieu S¹*, Ram-Wolff C¹, Quéreux G², Oro S³, Beylot-Barry M⁴, Aubin F⁵, Dalac S⁶, D'Incan M⁷, Verneuil L⁸, Bagot M¹, Groupe Français d'Etude des Lymphomes Cutanés (GFELC)

¹Hôpital Saint-Louis, APHP, Paris, France; ²CHU Nantes, Nantes, France; ³CHU Henri Mondor, APHP, Créteil, France; ⁴CHU Bordeaux, Bordeaux, France; ⁵CHU Besançon, Besançon, France; ⁶CHU Dijon-Bourgogne, Dijon, France; ⁷CHU Clermont-Ferrand, Clermont-Ferrand, France; ⁸CHU Caen, Caen, France

INTRODUCTION: Brentuximab Vedotin (BV) is a human monoclonal anti-CD30 antibody coupled to monomethylauristatin. We report 32 cases of mycosis fungoides (MF) and Sézary syndrome (SS) treated with BV and describe adverse effects (AE) and efficacy. METHODS: Members of the « Groupe Français d'Etude des Lymphomes Cutanés » (GFELC) completed questionnaires regarding patients using BV from November 1st 2012 to December 31st 2015.

RESULTS: 20 men (62%) and 12 women (38%), average age 66, from 8 French hospitals were included in this retrospective multicentric study. 19 patients (60%) had MF, 10 (31%) SS and 3 (9%) another T cell lymphoma. The disease had evolved for 7.4 years in average. The stage at the introduction of BV was: IB 3 cases, IIB 9, IIIA 4, IIIB 1, IVA1 5, IVA2 4 and IVB 4. 2 were not MF or SS. 22 (69%) displayed cytologic transformation. The cutaneous lymphocytic infiltrate expressed CD30 in most cases. Patients received 2 to 14 lines of treatment prior to BV. Patients received an average of 4.8 cycles of BV at a dose of 1,8 mg/kg IV every 3 weeks. 17 (53%) patients had AE, most frequently neuropathy (7/22%), nausea (5/16%), skin rash (4/13%) and diarrhea (4/13%). BV induced complete remission (CR) in 5 patients (16%), partial response (PR) in 11 (34%). The disease remained stable in 7 (22%) and progression occured in 9 (28%). 8 (25%) in CR or PR were able to undergo an allogeneic bone marrow graft. A phase II clinical trial of BV published by Kim et al, reported a 70% response rate. Duvic et al, reported a 53% response rate. We report 50%. They report 65% of peripheral neuropathies and we report 22%. They also report fatigue, skin rashes, diarrhea and neutropenia more often than we do. Their patients received 6 to 7.5 cycles in average, versus 4.8 in our study.

CONCLUSIONS: Our series confirms the efficacy of BV in the treatment of resistant MF and SS with an acceptable tolerability profile. BV is mostly used to induce remission allowing an allogeneic bone marrow graft.

$\label{eq:posterior} P-05 EVALUATION OF TREATMENT IN INDOLENT AND AGGRESSIVE SUBGROUPS OF FOLLICULOTROPIC MYCOSISFUNGOIDES$

ORAL van Santen S*, Vermeer MH, Willemze R | Leiden University Medical Center (Leiden, the Netherlands)

INTRODUCTION: Folliculotropic mycosis fungoides (FMF) is recognized as a distinct variant of mycosis fungoides (MF) which generally runs a more aggressive clinical course and is less responsive to standard skin-directed therapies (SDT). Recent studies suggested clinicopathologic criteria allowing distinction between an indolent (early stage FMF) and a more aggressive (advanced stage FMF) subgroup (10-year disease specific survival 93% vs. 40%, respectively). In the present study the results of initial treatment after diagnosis in a large cohort of patients presenting with early or advanced stage skin-limited FMF were evaluated.

METHODS:186 Patients presenting with skin-limited FMF (84 early stage FMF, 102 advanced stage FMF), included in the Dutch Cutaneous Lymphoma Registry between 1985 and 2014 were studied. Type and result of initial treatment after diagnosis were retrieved from the Dutch Registry and medical records. Main outcomes were complete remission (CR), sustained complete remission (SCR), partial response (>50% improvement; PR) and overall response (OR; CR+PR).

RESULTS: Patients with early stage FMF had mainly been treated with non-aggressive SDT (67 of 84 cases) resulting in CR and OR of 28% and 83% for monotherapy topical steroids, 0% and 83% for UVB and 30% and 88% for PUVA, respectively. In patients with advanced stage FMF these SDT were less effective (combined RESULTS: CR and OR: 10% and 52%, respectively). In patients with advanced stage FMF local radiotherapy (CR 63%; OR: 100%), total skin electron beam irradiation (CR: 59%; OR: 100%) and PUVA combined with local radiotherapy (CR: 5%; OR: 75%) were most effective.

CONCLUSIONS: Our results indicate that patients with early stage FMF may benefit from SDT (similar to early stage classical MF), whereas patients with advanced stage FMF require more aggressive treatment approaches.

P-06 TREATMENT OF EARLY-STAGE FOLLICULOTROPIC MYCOSIS FUNGOIDES: A SINGLE-CENTER EXPERIENCE

ORAL Amitay-Laish I*1,3, A¹, Prag-Naveh H¹, Pavlovsky L^{1,3}, Feinmesser M^{2,3}, Hodak E^{1,3}

Departments of ¹Dermatology, and ²Pathology, Rabin Medical Center - Beilinson Hospital, Petach Tikva, and ³Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

INTRODUCTION: Folliculotropic mycosis fungoides (FMF) may present as an early disease with an indolent course, as recently reported. Yet, even in early-stage FMF, the disease epicenter is deeper than in classic MF. There are no treatment recommendations specifically for early-stage FMF. Objectives: To report our experience with treatment of early-stage FMF, with emphasis on pso-ralen+ultraviolet A (PUVA) as monotherapy.

METHODS: Thirty-nine adults with early-stage FMF (IA-IIA), manifested by follicle-based patches/flat plaques and/or keratosis pilaris-like and/or acneiform lesions with/without alopecia, were treated and followed from January 1995 through June 2016. Data on 15 patients with well-defined classic early-stage MF given PUVA monotherapy, served for comparison.

RESULTS: Twenty-four of the 39 patients with FMF, (11-IA, 13-IB), received PUVA monotherapy, either at outset (n=20) or after failure of narrowband ultraviolet B (NB UVB)/UVA+UVB (n=4). Complete response (CR) was achieved in 17/24 (70%) after a mean of

Scientific Session P: Clinical Management & Challenging Cases

59 treatments (median 52, range 30-116). By comparison, of the 15 classic early-stage MF, treated with PUVA monotherapy at our department, 87% achieved CR (p=0.44), after a mean of 36 treatments (p<0.01) (median 39, range 24-50). CR was achieved in 9/11 patients with FMF IA (82%) and 8/13 (61%) with stage IB (p=0.39), with no significant difference from rates of staged-based classic MF. Mean number of treatments to CR was 49 for FMF IA and 30 for classic MF IA (p=0.048); values for stage IB FMF and classic MF IB were 71 and 38, respectively (p<0.01). Of the remaining 15 patients with FMF, initial treatment consisted of NB UVB (n=3; CR-1, stable disease-2), NB UVB+UVA (n=2; CR-1, stable disease-1), PUVA+interferon- α (n=2; CR-2), topical mechlorethamine (n=2; partial response-1, progressive disease-1), and isotretinoin, methotrexate, localized electron beam, PUVA-bath, or interferon- α (1 each). At the last follow-up (mean 84 months, range 8-240), 16 patients had no evidence of disease, 17 had minimal disease, and 5 had significant disease with progression to ≥IIB in 3 (8%); 1 patient died of disease.

CONCLUSIONS: PUVA may be effective monotherapy for early-stage FMF in adults. A higher number of treatments are needed to achieve CR than for classic MF.

P-07 FOLLICULOTROPIC MYCOSIS FUNGOIDES: A CASE SERIES STUDY

POSTER Abeldaño A*, Arias M, Nicola L, Benedetti A, Maskin M, Trila C Hospital General de Agudos Dr. Cosme Argerich, Buenos Aires, ARGENTINA

INTRODUCTION: Folliculotropic mycosis fungoides (FMF) is an uncommon subtype of mycosis fungoides with distinct clinical and histological features, a more aggressive course, less therapeutic responses and worse prognosis when compared to classical MF. Objectives: To evaluate the clinical and histological features, therapeutic responses and outcomes in patients with FMF in a single center in Argentina.

METHODS: A single-center observational, descriptive, retrospective study. FMF cases were selected from a database registry from November 1995 to September 2015.

RESULTS: Among 217 patients with primary cutaneous lymphoma, 84% were MF. We found 48 cases of atypical variants of MF. FMF was the most frequent subtype (n=24, 14%). Sixty two % of patients were male (M:F ratio 1.7:1). Mean age at diagnosis 55 years (23-82 years). Four patients had a previous diagnosis of classical MF. Average follow-up time: 54 months. The most common sites of involvement were trunk (73%), and head and neck (55%). Clinical presentation: plaques (85%), follicular keratototic papules (77%), tumors (55%), acneiform lesions (comedo-like and epidermal cysts) (19%) and alopecia (14%). The main symptom was pruritus. Histopathological findings included infiltration of the follicular epithelium by atypical lymphocytes in all cases. Mucinous degeneration of the follicular epithelium was found in 62% (15/24) of cases. Inmunohistochemical analysis showed a mature, T-helper phenotype with CD3+, CD4+ and CD8-. Staging: 75% had advanced stage disease (IIB-IVA). Only 6 patients (25%) were in the early stage (IA-IB). All patients received combination therapy with PUVA, interferon alpha, bexarotene, local radiotherapy, total skin electron beam. A complete response was achieved in only 12% of cases. Disease progression was observed in 7 patients (29%): 6 evolved to a transformed MF. Among them, most patients had advanced stage disease at diagnosis (IIB). Eight patients died related to their disease. CONCLUSIONS: FMF was the more common variant among unusual MF subtypes. Since most of the patients were in advanced stages at diagnosis, it was associated with a lower response to initial treatment and further progression of the disease. For this type of MF with worse prognosis, more aggressive therapeutic alternatives should be considered.

P-08 EARLY STAGE FOLLICULOTROPIC MYCOSIS FUNGOIDES ASSOCIATED WITH EOSINOPHILIC PNEUMONIA

POSTER Ohmatsu H*1, Takahashi K1, Hayashi Y1, Takimoto S1, Miyake A1, Horita A2, Saito I2

¹Department of Dermatology, Sagamihara National Hospital, Kanagawa, Japan; ²Department of Diagnostic Pathology, Sagamihara National Hospital, Kanagawa, Japan

INTRODUCTION: Folliculotropic mycosis fungoides (FMF) is the most common variant of mycosis fungoides (MF) characterized by the presence of folliculotropism and preferential involvement of the head and neck area. FMF was reported to show a poor prognosis compared to classic MF. Recently, FMF has been proposed to present with two distinct patterns of clinicopathologic features with different prognostic implications representing the early stage and the advanced stage FMF. Early stage FMF does not always have tumors/nodules on the neck and head area, but often presents patches/ acneiform lesions on the trunk and limbs. METHODS: Here, we present an early stage FMF patient with eosinophilic pneumonia.

RESULTS: A 76-year-old Japanese man suffering from severe pruritus for 3 years presented to our department. His past medical history was chronic obstructive pulmonary disease. Diagnosed with chronic eczema by his previous doctor, he was treated with topical and systemic steroids. Physical examination revealed some folliculitis on his back. No involvement of lymph nodes or visceral organs was found. Therefore, we did not think the possibility of cutaneous lymphoma at that point. After discontinuance of systemic steroids, he took cyclosporin for about one year. Although pruritus persisted, almost no eruptions took place during the treatment with cyclosporin. Since eosinophil counts and the titer of sIL-2R went up to 2700/ul and 1700U/ml, respectively, he discontinued cyclosporin. After that, multiple edematous erythemas occurred on his limbs and trunk. Skin specimen taken from the erythema revealed epidermotropism and mild folliculotropism. Infiltrating lymphocytes were CD3+, CD4+ and CD8-. We diagnosed him with early stage FMF. After two months later, he had a high fever and was diagnosed with eosinophilic pneumonia with a computed tomography.

CONCLUSIONS: Hypereosinophilia is often detected in MF related to a poor prognosis, however the association between MF and eosinophilic pneumonia is not common. To the best of our knowledge, there is only one report of eosinophilic pneumonia associ-

Scientific Session P: Clinical Management & Challenging Cases

ated with cutaneous T-cell lymphoma. Cyclosporin would induce activation of eosinophils in this patient. It is the first report of FMF with eosinophilic pneumonia.

P-09 SPONTANEOUS REMISSION OF A PYOGENIC VARIANT OF A PRIMARY CUTANEOUS CD30+ ANAPLASTIC LARGE CELL LYMPHOMA IN A YOUNG MAN

POSTER Geissler E*, Hees H, Dippel E | Klinikum Ludwigshafen, Department of Dermatology, 67063 Ludwigshafen, Germany

Differentiating the cutaneous CD30+ T cell lymphoma entities is often a diagnostic challenge whereas they are accompanied with an excellent prognosis. A pyogenic variant of a primary cutaneous anaplastic large cell lymphoma is described, which shows a high tendency to spontaneous remission although the clinical findings are impressive. A 20-year-old man presented with a fast growing tumor lesion of the face. The magnetic resonance imaging showed considerable swelling of the whole left cheek and significant lymph node enlargement. A regression tendency was shown during work-up and diagnostics so that we decided to delay a targeted therapy or radiotherapy. The lesion showed a complete remission after only two weeks. Even during the last follow-up one year since the first finding, a complete remission has still occurred. The histology of a skin biopsy showed a wide infiltrate of neutrophils and a diffuse infiltration of tumor cells under a profound necrotizing epithelium defect. The neoplastic infiltration consisted of medium size blast clonal cells which showed among others positivity for CD3 and CD30. Cutaneous CD30+ lymphoproliferative disorders comprise a heterogeneous group of diseases with respect to outcome, clinical presentation and histologic features. A described pyogenic variant is presenting with purulent nodules and histologically with strong infiltration with neutrophils. This form usually appears on younger patients and suggests an aggressive clinical course. Interestingly it shows an excellent outcome. Regarding the treatment regimens, the high rate of spontaneous remission of all CD 30+ cutaneous lymphomas should be considered. After eliminating a systemic involvement, the indication of "watchful waiting" should be placed. In our case, the patient showed a regression tendency during work-up and diagnostics. This is often described and is important for therapeutic and prognostic purposes. The pyogenic variant of a primary cutaneous anaplastic large cell lymphoma frequently presents aggressive clinical findings in spite of having an excellent prognosis. The diagnostic and treatment regimens are often a challenge in managing this type of lymphoma since there is often pressure to treat on behalf of the patients.

P-10 REGRESSION OF A CD30-POSITIVE PRIMARY CUTANEOUS T-CELL LYMPHOPROLIFERATION AFTER RIBAVIRIN TREATMENT OF CHRONIC HEPATITIS E VIRUS INFECTION

POSTER Laroche L^{*1}, Bruneau J^{2,3}, Zuber J^{3,4}, Aliano C⁵, Leclerc-Mercier S², Belaid Z⁶, Kraft A⁷, Roulot D⁸, Roque AM⁹, Wedemeyer H⁷, Pol S¹⁰, Hillon P¹¹, Hermine O¹², Mallet V^{3,10}

¹Assistance Publique des Hôpitaux de Paris (APHP), Hôpital Avicenne, Dermatology Department, University of Paris 13, Bobigny, France; ²APHP, Hôpital Necker, Pathology Department, Paris, France; ³Université Paris Descartes, Paris, France; ⁴APHP, Hôpital Necker, Renal Transplantation Department, Paris, France; ⁵Institut Pasteur, France; ⁶Institut Imagine, INSERM U 1163 / CNRS ERL 8254, Paris, France; ⁷Gastroenterology, Hepatology, Endocrinology, Hannover Medical School, Hannover, Germany; ⁸APHP, Hôpital Avicenne, Gastroenterology Department, University of Paris 13, Bobigny, France; ⁹APHP, Hôpital Paul Brousse, Virology Department, Paris, France; ¹⁰APHP, Hôpital Cochin, Hepatology Department, Paris, France; ¹¹Hôpital Bocage,, Gastroenterology Hepatology Department, Dijon, France; ¹²APHP, Hôpital Necker, Hematology Department, Paris, France

Pathogenesis of primary cutaneous CD30+ T cell lymphoproliferative disorders is not clearly elucidated. Viral infection has been proposed as causative cofactors in these diseases. We report here a unique case of concurrent primary cutaneous CD30+ T-cell lymphoproliferative disorder and chronic hepatitis E virus (HEV) infection, its clinical course paralleling the viral response. A 62-year old Caucasian male was diagnosed with a typical type B lymphomatoid papulosis in 2005 and subsequently with chronic HEV (genotype 3c) infection and cirrhosis in 2009. He was treated chronologically in March 2010 with ribavirin for 12 weeks, in February 2011 with ribavirin for 48 weeks then with ribavirin and interferon (as an add-on) for 40 weeks, and in May 2013 with ribavirin and interferon for 48 weeks. Remarkably, skin lesions and hematological responses paralleled the virological response. The patient remained free of any cutaneous lesion after achieving a sustained virological response. Skin biopsies and a complete hematological workup were carried out between the second and the third treatment. The immunological workup did not detect any common cause of primary or acquired immune deficiency. Cutaneous T cell proliferation consisted of scattered large CD30+ lymphocytes surrounding blood vessels within a predominant small CD8+ infiltrate. Restricted usage of TCR V-beta of infiltrating cells was consistent with oligoclonal expansion. HEV core protein and RNA were readily detected in endothelial cells by immunofluorescence and in-situ hybridization, respectively. Furthermore, viral-like particles were detected in endothelial cells using electronic microscopy. The data show for the first time a possible role of HEV infection in the pathogenesis of LyP. Extrahepatic replication sites, including skin endothelial cells, will be discussed as well as its association with CD30+ T-cell lymphoproliferative disorders. HEV screening should be part of the workup of any lymphoproliferative disorder.

P-11 A CASE OF PRIMARY CUTANEOUS ANAPLASTIC LARGE CELL LYMPHOMA ALK- NEGATIVE

POSTER Khatami R*, Wang Y, Ahmed Ti | Department of Pathology, Stony Brook Medicine, Stony Brook, New York

Anaplastic large cell lymphoma (ALCL) is a rare type of NHL, but the second or third most common subtype of T-cell lymphoma. Approximately 10 percent of the time, primary cutaneous ALCL extends beyond the skin to lymph nodes or organs. If this occurs, it

Scientific Session P: Clinical Management & Challenging Cases

is usually managed like the systemic forms of ALCL. We present a case of an ALK negative primary cutaneous ALCL who presented with diffuse cellulitis and was subsequently found to have extensive lymph node involvement on autopsy. The patient is a 62 year old male with a medical history of depression, urothelial cell carcinoma S/P TURBT, morbid obesity, diabetes, recurrent abscess formations, and obstructive sleep apnea who presented to another hospital with left chest cellulitis with lymphadenopathy. His clinical course was complicated by poor wound healing and high serum IgE (37000 Units/mL), he was transferred to our facility. Skin and soft tissue biopsy showed anaplastic large cell lymphoma. His clinical course was complicated by positive lymph nodes for metastatic anaplastic large cell lymphoma. The skin and soft tissue showed ulceration and extensive involvement by large atypical cells with hallmark cells positive for CD30,CD4 not CD8,CD43,and negative for ALK-1 consistent with anaplastic large cell lymphoma ALK- negative. Fluorescent in situ hybridization performed on a paraffin embedded slide showed the presence of 3-6 copies of 2p23 (ALK region) of chromosome 2 but not translocation 2:5. Patient was not treated due to his poor performance status. This case presents diagnostic difficulties as Cutaneous ALCL may resemble a cellulitis or recurrent abscess.

P-12 PROLONGED SURVIVAL IN A 46-YEAR-OLD MALE PATIENT WITH CUTANEOUS GAMMA/DELTA T-CELL LYMPHOMA POSTER Sagher E*, Stevens E, Chan M, Tejasvi T | University of Michigan Department of Dermatology, Ann Arbor, Michigan, USA

Cutaneous gamma/delta T-cell lymphoma is a rare lymphoma composed of a clonal proliferation of activated gamma/delta T-cells with a cytotoxic phenotype. The prognosis of patients with this disease is grim, with a median survival of 15 months. We report the case of a 46-year-old male with a 30-month disease history, who improved with treatment. This individual presented with a one-year history of rapidly progressive large exophytic ulcerated masses on the right thigh and right buttocks, as well as diffuse pruritic scaly patches and plaques on his trunk, upper, and lower extremities. He had significant lymphadenopathy of the right inguinal group and had no organomegaly. Biopsy demonstrated pandermal infiltrate of atypical lymphoid cells positive for CD2, CD3, CD5, CD7, CD56, TIA-1, granzyme B, and TCR gamma delta. The clinical picture and immunophenotype were consistent with cutaneous gamma/delta T-cell lymphoma, and he was subsequently admitted for modified Goeckerman. PET-CT revealed FDG activity of the right hip, right inguinal region, and back, and right inguinal lymph node biopsy was consistent with this aggressive type of CTCL. Upon discharge, he received radiation therapy, topical steroids, CHOP combination chemotherapy, with improvement in his disease. His course is notable for a flare that required a second admission for modified Goeckerman with PUVA. In conclusion, cutaneous gamma/delta T-cell lymphoma is a difficult disease to treat because of its aggressiveness and resistance to multiagent chemotherapy and radiation, so his improvement and length of survival is unusual, but relapses such as these unfortunately are not. With this in mind, he follows closely with the bone marrow transplant team, as allogeneic hematopoietic stem cell transplantation is an option for refractory disease.

P-13 ANAPLASTIC LARGE CELL LYMPHOMA INVOLVING SKIN AND MUSCLE ASSOCIATED WITH POLYMYOSITIS

POSTER Miyagaki T¹*, Sugaya M¹, Hayashi Y¹, Nakamura K¹, Takahashi N¹, Asano Y¹, Sato S¹, Koguchi A², Yamaguchi N², Ueda J², Shimizu J², Tsuji S², Taoka K³, Kurokawa M³

¹Department of Dermatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; ²Department of Neurology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; ³Department of Hematology and Oncology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

There is a well-documented association between autoimmune inflammatory myopathies and several malignancies. Among hematologic malignancies, B-cell lymphomas are more commonly reported than T-cell lymphomas. Here we report a rare case of anaplastic large cell lymphoma (ALCL) involving skin and muscle associated with polymyositis. A 32-year-old Japanese man was referred to our hospital with muscle weakness with elevated serum creatine kinase (CK) levels. Muscle biopsy of the biceps revealed inflammatory mononuclear cell infiltration within the endomysium and muscle fiber necrosis and regeneration. He was diagnosed as having polymyositis. He had been treated with oral prednisolone, intravenous gamma globulin, and oral immunosuppressant agents such as cyclosporine A, tacrolimus, or methotrexate, and his symptoms had improved moderately. After four years, muscle weakness exacerbated without elevation of serum CK levels. Scattered erythematous plaques and nodules with occasional ulceration and several intramuscular nodules appeared. Biopsy specimens of both skin and intramuscular nodules revealed massive infiltration of mediumto large-sized atypical lymphocytes. They were positive for CD3 and CD30, and negative for CD20, CD56, or EBER. Monoclonal T cell receptor (TCR) rearrangement was detected in both skin and intramuscular nodules. As the same TCR rearrangement peak and infiltration of a small number of CD30-positive lymphocytes in muscle fiber were found in the first muscle biopsy specimen, we diagnosed him as having ALCL involving skin and muscle, which exacerbated after 4 years of immunosuppressive therapy. As muscle weakness continued in spite of cessation of oral methotrexate, he is now treated with CHOP therapy. Muscle weakness is gradually improving. Muscle weakness can be caused by malignant lymphoma. It is important to consider the coexistence of malignant lymphoma when examining the patients with autoimmune myopathies. If there are skin eruptions apart from typical ones of dermatomyositis, skin biopsy can be useful to make the right diagnosis.

P-14 A CASE OF ANGIOINVASIVE CUTANEOUS ANAPLASTIC LARGE CELL LYMPHOMA COMPLETELY REGRESSED AFTER LOW DOSE SYSTEMIC METHOTREXATE

POSTER Russo I*, Ferrazzi A, D'Amore ES, Alaibac M | Unit of Dermatology, University of Padua, Padua, Italy

107

Scientific Session P: Clinical Management & Challenging Cases

Primary cutaneous CD30+ lymphoproliferative disorders are the second most common type of cutaneous T cell lymphoma and include lymphomatoid papulosis and anaplastic large cell lymphoma. Five types (A,B,C,D,E) of lymphomatoid papulosis with different histopathological and clinical features have been described. Lymphomatoid papulosis type E typically shows an angioinvasive pattern and presents with eschar-like ulcers. This condition should be separate from a variant of cutaneous anaplastic large cell lymphoma characterized by a similar angioinvasive pattern and clinical presentation that have been recently described. Treatment of lymphomatoid papulosis usually involves low-dose methotrexate and UV Phototherapy, whereas localized radiotherapy and surgical excision are commonly used for the treatment of cutaneous anaplastic large cell lymphoma. Here we report a case of primary cutaneous anaplastic large cell lymphoma with angioinvasive features completely regressing after low dose methotrexate therapy.

P-15 A CASE OF SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA ASSOCIATED WITH HEMOPHAGOCYTIC SYN-DROME

POSTER Balakrishnan D*, Ahmed T | Stony Brook University Hospital, Stony Brook, New York

Subcutaneous panniculitis-like T cell lymphoma (SPTCL) is a peripheral T cell lymphoma which is derived from a mature cytotoxic T cell that accounts for less than 1% of non-Hodgkin's Lymphoma and commonly mimics panniculitis. Less than 20% of cases are associated with hemophagocytic syndrome (HS). We present a case of SPTCL associated with HS. A 27 year-old woman who presented at our institution with high fevers, diffuse painful subcutaneous nodules and myalgia in July 31, 2014. Lab findings on admission showed anemia (Hb: 11.2 g/dL), leukopenia (2.65 K/uL) and elevated AST (39 IU/L). CT imaging revealed numerous ill-defined nodular opacities in the subcutaneous fat of the anterior abdominal wall, flanks, medial aspect of breasts bilaterally and paraspinous region without overlying cutaneous lesions. After a soft tissue biopsy of the nodules was performed the patient was discharged home. The biopsy showed SPTCL. She was readmitted three weeks later with unresolved symptoms. However, new lab findings revealed increased elevated liver enzymes (ALT 75 IU/L and AST 175 IU/L). Ferritin levels were also high and continued to increase dramatically over the next few days from (579.9 to 29257 ng/ml). Other labs revealed anemia (Hb 9.6 g/dL), elevated triglycerides (265 mg/dL) and low NK cell activity. A bone marrow biopsy performed on August 29, 2014 showed a normocellular bone marrow with hemophagocytosis. The findings were consistent with hemophagocytic syndrome in a setting of SPTCL. The soft tissue biopsy showed a population of atypical cells which stained positive for CD3, CD8 and TiA1 and negative for CD56. CD5 was partially lost on the atypical cells. TCRy was positive on a subset of the atypical cells. These findings support a diagnosis of SPTCL.

T-Cell gene rearrangement studies showed 90-95% of all TRG gene rearrangements occurring in the clonal T-Cell population. The patient was started on Doxil in September 2014 with good initial response but was soon lost to follow-up. This case highlights the importance of considering the occurrence of rare syndromes in the presence of rarer diagnoses.

P-16 LIVEDOID VASCULOPATHY AS A POSSIBLE CLINICAL PRESENTATION OF PRIMARY CUTANEOUS LYMPHOMA WITH A T REGULATORY PHETOTYPE.

POSTER Alberti-Violetti S¹, Bagnoli F², Corti L¹, Fanoni D¹, Valentina M¹, Luigia V², Berti E^{*1,2}

¹Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Dermatology, Milan (Italy); ²Università degli Studi di Milano, Milan (Italy)

Forkhead box protein 3-positive (FoxP3+) T cell lymphoma, in the absence of human T cell lymphotrophic virus type 1 (HTLV-1) infection, is rare and its clinicopathological characteristics still remain unclear. We describe a very rare case of a primary cutaneous lymphoma characterized by T-reg phenotype, systemic involvement and a long history of livedoid vasculopathy presenting a T-cell clone identical to the lymphoma. We describe the case of a 48-year-old caucasian woman with a 24-year history of idiopathic widespread livedoid vasculopathy, treated with several immunosuppressive agents with partial response. She presented new multiple plagues localized on the face. We performed skin biopsies to study histopathological and immunohistochemical characteristics. T-cell receptor-gamma (TCR) gene rearrangement was evaluated using Polymerase chain reaction and Gene Scan analysis with BIOMED-2 standardized protocol. Genomic alterations were evaluated by array-comparative genomic hybridization (a-CGH). Routine blood tests were normal, except for trombocytosis. Skin biopsies revealed a dense multinodular angiocentric infiltrate mainly composed of small/medium-size pleomorphic cells and eosinophils. Neoplastic cells showed a CD4+ CD25+ FOXP3+ phenotype. HTLV-1 serology was negative. An identical T-cell clone in the new lymphoproliferative lesions and in the old vasculopathic lesions was found. Staging was negative. A-CGH analysis revealed losses on chromosome 8p11.2. During follow up, an atypical FOXP3+ lymphoid infiltrate with the identical T-clone to the skin was also found in the lymph nodes, as well as bone marrow. The patient was initially treated with mono-chemotherapy (cyclophosphamide, and then chlorambucil) with progression to the liver. The patient died for multiorgan failure. This is a very rare and interesting case of FOXP3+ T cell lymphoma, with a primary cutaneous involvement in absence of HTLV1 infection. Interestingly, the patient had a long history of idiopathic widespread livedoid vasculopathy characterized by an identical T clone to the lymphoproliferative lesions. Considering that detection of a dominant T-cell population had raised the hypothesis that some angioproliferative processes like angiolymphoid hyperplasia with eosinophilia might be an early form of T-cell lymphoma, we postulate that in our patient livedoid vasculopathy might represent precursor lesions of the lymphoma.

P-17 PRIMARY CUTANEOUS FOLLICLE CENTER LYMPHOMA PRESENTING AS DIFFUSE ALOPECIA

POSTER Chung CG*, Hallock K, Lawson C Penn State Health Hershey Medical Center, Hershey, PA, USA; Dermatology Associates of Lancaster, Lancaster, PA, USA
Abstracts

Scientific Session P: Clinical Management & Challenging Cases

Primary cutaneous follicle center lymphoma (PCFCL) is an indolent primary cutaneous B-cell lymphoma composed of neoplastic follicle center cells. PCFCL typically presents with erythematous to violaceous papules, nodules, and plaques on the head, trunk, and less commonly extremities. Alopecia is not a characteristic finding. The authors describe an unusual case of primary cutaneous follicle center lymphoma in a 78-year-old woman presenting with a 2-month history of progressive diffuse non-scarring alopecia. No induration or palpable masses were present. Skin biopsy from the scalp revealed a nodular proliferation of B lymphocytes with histopathologic and immunophenotypic findings most consistent with PCFCL. Systemic evaluation including complete blood count, lactate dehydrogenase, peripheral blood flow cytometry, whole-body PET/CT, and bone marrow biopsy did not reveal any evidence of internal disease. The patient was treated with systemic rituximab with improvement of her hair loss.

P-18 TELANGIECTATIC ERYTHEMA INDUCED BY MECHLORETHAMINE GEL (VALCHLOR)

POSTER Maubec E*1, Levy A², Laroche L¹

¹Assistance Publique des Hôpitaux de Paris (APHP), Hôpital Avicenne, Dermatology Department, University of Paris 13, Bobigny, France; ²APHP, Hôpital Avicenne, Pathology Department, Bobigny, France

Mechlorethamine gel is used as a topical drug for Mycosis Fungoides (MF). Most common adverse events include skin irritation, pruritus, erythema, contact dermatitis and skin hyperpigmentation. We report a series of 3 cases of telangiectatic erythema induced by mechlorethamine gel. A 54-year-old woman with stage IA MF was administrated, as 3rd line treatment, mechlorethamine gel once a day on flank and breast patches. Two months later, patches were replaced by telangiectatic erythema. Mechlorethamine was then applied 3 times a week, with slow erythema disappearance in 2 months. A 51-year-old woman with Sezary syndrome was treated by mechlorethamine gel, 3 times a week. At week 3, she presented with generalized telangiectatic erythema. Mechlorethamine gel was discontinued at week 5. Erythema slowly disappeared in 2 months. A 68-year-old man with stage T2 MF was administered mechlorethamine gel twice a week. Two months later, the treatment was stopped because of a generalized ulcerated telangiectatic erythema. Mechlorethamine disappeared in 2/2 patients. We report for the first time a series of 3 cases of mechlorethamine gel- induced telangiectasia erythema. Among topical alkylating agents, only carmustine has been shown to induce telangiectasia. In contrast, mechlorethamine in aqueous solution (Caryolysin) has never been reported to induce telangiectasia. This unexpected adverse event of mechlorethamine gel might be related to its pharmaceutical form (gel vs aqueous solution) or/and to its concentration on the skin. Another hypothesis might be genetic polymorphisms involved in the oxidative stress or ATM pathway, as reported in radiation induced telangiectasia. This adverse effect should be known by physicians who should notify patients, especially if treated surface area is large.

P-19 PRALATREXATE ASSOCIATED SKIN NECROSIS: A POTENTIAL SEVERE ADVERSE EFFECT

POSTER Ko J¹, Rosman I¹, Scaeffer A¹, McHargue C², Carson K¹, Musiek A¹

¹Washington University in St. Louis School of Medicine; St. Louis, MO, ²Henry Ford Health System; Detroit, MI

Pralatrexate is an antifolate approved in 2009 by the US FDA for the treatment of peripheral T-cell lymphoma. In this case series, we will describe four cases of pralatrexate associated skin necrosis and compare features of time to presentation, clinical presentation, pathology, presence of leucovorin rescue and other associated adverse effects. A 69 year-old man with history of mycosis fungoides presented to Barnes Jewish Hospital with a new-onset diffuse rash associated with burning and itching. Four days prior to admission, he had been started on four medications, pralatrexate, prochlorperazine, allopurinol, and terbinafine. On initial examination, the patient had diffuse erythematous macules and papules coalescing into patches over his entire body. Given the new onset of the rash in relation to medication initiation, a diagnosis of morbilliform drug eruption secondary to medication was considered. Pralatrexate, allopurinol, and terbinafine were held and oral prednisone taper and topical steroids to affected areas was initiated. Subsequent examinations revealed superficial erosions with yellow drainage that worsened to full thickness skin sloughing with a denuded red base. He also developed vermilion lips with hemorrhagic crusting along with areas of erythema with easily scrapeable yellow and white papules in the oral mucosa. Wound care was initiated and topical steroids were discontinued. Due to concern for possible SJS, punch biopsy was obtained from an area of rash on the hip which showed epidermal dysmaturation and interface dermatitis more consistent with a toxic reaction to a chemotherapeutic agent. His oral ulcerations worsened to the point of difficulty breathing requiring intubation and he developed a neutropenic fever requiring transfer to the ICU. He subsequently developed respiratory failure secondary to pneumonia leading to septic shock. After discussion with family members, comfort care measures were initiated and the patient died one week later. These cases highlight a potential severe adverse reaction mimicking toxic epidermal necrolysis to pralatrexate that has not been previously reported in detail. While this adverse effect appears to be rare, clinicians should be aware of the association of pralatrexate with this adverse effect.

P-20 HAIR AND NAIL CHANGES IN PATIENTS WITH MYCOSIS FUNGOIDES FOLLOWING TOTAL SKIN IRRADIATION POSTER Breneman A, Breneman DL*, Ballman E, Breneman JCi | University of Cincinnati College of Medicine, Cincinnati, Ohio

INTRODUCTION: Total Skin Irradiation (TSI) is an effective method of treatment for patients with Mycosis Fungoides (MF), but use of this treatment has been limited by concerns of potential toxicities. The purpose of this study is to document the risk of permanent hair loss and nail dystrophy after TSI administered for treatment of MF.

METHODS: Fifteen patients with MF were treated with TSI. 3600 cGy was administered in 20 fractions. Combination radiation and

Abstracts

Scientific Session P: Clinical Management & Challenging Cases

chemotherapy was administered to two patients as part of a National Cancer Institute protocol. Based on history and physical examination, data was collected regarding hair and nail loss and regrowth at months 1, 6, 12, and 18.

RESULTS: Thirteen patients had 90% or greater loss of scalp hair during treatment, and new growth appeared approximately two months following treatment completion. After eighteen months, hair had regrown to approximately 70% of baseline thickness. Cosmetically obvious alopecia was not present in the group of patients treated with TSI alone. Two patients who were treated with TSI and CHOP chemotherapy. Both had substantially less regrowth of scalp hair with persistent cosmetically obvious alopecia. In some patients hair regrowth was darker (53.8%), finer (85%), and/or curlier (46.1%) than before treatment. Some loss of eyebrows (54%) and eyelashes (38%) developed, but complete regrowth occurred in all patients. Nails were lost an average of three months following treatment initiation and had regrown in most patients by five months after treatment completion (range 1-11 months). New nails were normal in 60% of patients, but a few patients developed stronger nails or post-therapy nail dystrophies.

CONCLUSIONS: The majority of patients treated with TSI alone did not develop long-term cosmetically obvious alopecia. However, patients treated with combination TSI and CHOP chemotherapy developed post-treatment long-term cosmetically obvious alopecia. Post-treatment long-term nail regrowth in most patients was normal. This data can be used to better inform patients of likely long-term changes of hair and nails following TSI.

P-21 TRANSIENT GYNECOMASTIA AS AN ADVERSE EFFECT OF TOTAL SKIN ELECTRON BEAM IRRADIATION FOR THE TREATMENT OF CUTANEOUS T-CELL LYMPHOMA

POSTER Breneman A, Breneman DL*, Van Horn JA, Breneman JC | University of Cincinnati College of Medicine, Cincinnati, Ohio

INTRODUCTION: Gynecomastia as an adverse effect of Total Skin Electron Beam Irradiation (TSEBI) has been described rarely in the literature. The purpose of this study was to determine a possible mechanism for the development of gynecomastia following TSEBI. METHODS: Free testosterone, total testosterone, follicle-stimulating hormone (FSH), and leutinzing hormone (LH) were measured in four patients at baseline, one month post-treatment, and four-to-six months late post-treatment following 3600 cGy TSEBI. Thermoluminescent dosimeter measurements of the groin were used to determine the amount of radiation to which the testes were exposed. Clinical examination of each patient was performed to assess the presence of gynecomastia.

RESULTS: One of four patients developed painful gynecomastia. Baseline hormone levels were normal or near normal in all patients for all measurements taken. All patients had significantly elevated post-treatment FSH levels (range 1.36-4.53 times upper normal limit). Late post-treatment FSH was elevated in three patients and was high normal in one patient. Testosterone and LH levels remained within normal limits in all patients.

CONCLUSIONS: FSH levels were elevated in all patients post-TSEBI. Though testosterone levels did not significantly change, elevated FSH levels may be an indicator of decreased total androgen production. The imbalance in androgens and estrogens could lead to gynecomastia in patients treated with TSEBI.

P-22 MAINTENANCE PHASE IN PUVA PHOTOTHERAPY OF EARLY STAGE MYCOSIS FUNGOIDES. A CRITICALLY AP-PRAISED TOPIC

POSTER Grandi V*1, Pileri A^{1, 2}, Delfino C¹, Pimpinelli N¹

¹Department of Surgery and Translational Medicine, Division of Dermatology, University of Florence, Florence, Italy; ²Department of Specialized, Diagnostic and Experimental Medicine, Division of Dermatology, University of Bologna, Bologna, Italy.

INTRODUCTION: PUVA therapy is actually the first choice in patients with early stage Mycosis Fungoides, but there is no universally approved guideline for PUVA schedule. Recently, it has been proposed the use of "maintenance phase", a progressive tapering of applications in order to reduce relapses or prolong relapse free interval. Although conceptually intriguing, maintenance phase may have back sides, as it may increase the risk of cumulative UV-related side effects. Aim of this study was to critically analyse literature evidences of benefits from maintenance therapy.

METHODS: We performed a systematic search using Pubmed, Embase, TRIP database. All articles were screened, including all studies inherent to Mycosis Fungoides treated with PUVA phototherapy, with a follow up of at least 6 months and with accurate data on clinical outcomes, as defined by ISCL/EORTC recommendations. We excluded studies without a direct comparison between patients who underwent maintenance treatment and those who discontinued after reaching complete remission.

RESULTS: Of 574 articles screened, three studies were included in final critical appraisal. Sanchez et al performed a prospective observational study; of 40 patients in complete remission, 27 received maintenance therapy and 13 had simple follow up. In a 28 months follow up, 12 patients relapsed. The comparison of relapse rate in maintenance vs non maintenance group showed no statistically significant difference (P=0.16). Hernandez et al performed a retrospective analysis. They registered 22 cases of complete remission, and 12 of these received maintenance therapy. 36% of patients relapsed during mean follow-up of 62 months. Comparing relapse free intervals in maintenance vs non maintenance group also showed no significant differences (P>0.1). Wackernagel et al analysed retrospectively patients treated with PUVA. they compared relapse rates and relapse free intervals between 27 patients that received maintenance and 13 who underwent strict follow-up only. They encounter high relapse rates in both groups, with no statistically significant differences (P= 0.64 for relapse ratio and P= 0.87 for relapse free interval)

CONCLUSIONS: There is inadequate evidence to support introduction of maintenance phase in PUVA regimen for early stage MF. There is urgent need to perform a randomized clinical trial able to demonstrate a possible benefit of maintenance regimen.

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O-04 (oral) Economidi A A-07 (poster) Eder J C-02 (oral) Ekonomaki E A-07 (poster) Ekonomidi A C-02 (oral) **El-Sayed MH** F-10 (poster) Elco C G-05 (oral) Elco CP G-02 (oral) G-06 (oral) Elder JT G-10 (poster) Eldershaw S E-12 (poster) Enz P D-05 (poster) Erdos G O-07 (oral) Espinet B B-06 (oral) Espinosa L B-06 (oral) Estes J G-10 (poster) Esteve J I-08 (poster) Estrach T B-06 (oral) C-02 (oral) C-03 (oral) I-08 (poster) O-08 (oral) Evison F C-01 (oral) C-02 (oral) Fabbro S C-03 (oral) Fabio A J-05 (oral) Falo LD Jr. B-04 (oral) O-07 (oral) Fanelli C L-03 (oral) Fanok MH G-04 (oral)

Fanoni D A-03 (oral) I-06 (oral) P-16 (poster) Farkas DK K-04 (oral) Federico M K-02 (oral) Feinmesser M A-05 (oral) P-06 (oral) Feldman T O-04 (oral) Fernández de Misa R O-08 (oral) Ferrando A G-07 (oral) M-07 (oral) Ferrazzi A P-14 (poster) Fierro MT C-03 (oral) Finnegan G O-05 (oral) Fite C I-05 (oral) K-03 (oral) Flanagan C G-09 (poster) Fling SP O-10 (oral) Flores E J-09 (poster) Flores-Bozo LR I-03 (oral) Fogli LK G-04 (oral) Foss F G-03 (oral) N-02 (oral) N-03 (oral) O-10 (oral) Foss FM K-02 (oral) O-04 (oral) Franck N H-11 (poster) Frattini MG B-07 (oral) M-07 (oral) French L

Frew J N-04 (oral) Fridmanis M D-05 (poster) Fu P M-04 (oral) Fujita H F-01 (oral) Fuschiotti P E-03 (oral) Galindo R G-10 (poster) Gallardo F B-06 (oral) O-08 (oral) García A I-08 (poster) García L B-06 (oral) Garcia Pazos ML D-05 (poster) Garcia S G-02 (oral) Gargallo V C-02 (oral) Gaulard P I-07 (oral) Gehad A G-05 (oral) G-06 (oral) Gehr G N-13 (poster) Geissinger E L-02 (oral) Geissler E P-09 (poster) Georgakopoulos J P-02 (oral) Géraud C M-01 (oral) Geskin LJ B-04 (oral) B-07 (oral) E-03 (oral) G-07 (oral) J-01 (oral) M-07 (oral) O-05 (oral) Gill R M-05 (oral) Girardi M A-02 (oral)

E-08 (oral)

G-03 (oral) N-02 (oral) N-03 (oral) Gisselbrecht C K-02 (oral) Gitlin SD G-10 (poster) **Gkontopoulos K** M-11 (oral) Gleń J E-11 (poster) Glezou I M-11 (oral) Gniadecki R B-02 (oral) K-05 (oral) L-01 (oral) Goebeler M L-02 (oral) Goel S G-04 (oral) Goerdt S M-01 (oral) Goldfeiz N M-09 (oral) Gómez de la Cámara A O-08 (oral) Gonzaga Y N-06 (poster) Gonzalez BR E-01 (oral) González J B-06 (oral) Gordon GS M-02 (oral) Gorovitz B A-05 (oral) M-09 (oral) Grandi V C-03 (oral) E-06 (oral) P-22 (poster) Grange F H-04 (oral) H-11 (poster) O-06 (oral) Green R K-07 (poster) Grieve R N-04 (oral) Gru AA C-01 (oral)

C-04 (oral) Guan L M-04 (oral) Guenova E C-02 (oral) E-08 (oral) Guenova-Hotzenecker E K-05 (oral) Guitart J A-02 (oral) A-04 (oral) C-01 (oral) C-03 (oral) C-04 (oral) H-10 (poster) K-01 (oral) Gülow K M-01 (oral) Guyot A H-07 (poster) Haider A B-05 (oral) F-06 (oral) Hainaut Wierzbicka E N-05 (oral) Haioun C I-07 (oral) Hallock K P-17 (poster) Halpern I D-02 (oral) Hamada T F-08 (oral) Hamm S M-10 (oral) Hao Y M-12 (oral) Hayashi Y P-08 (poster) P-13 (poster) Hayden MS L-06 (oral) Hees H P-09 (poster) Heguy A G-04 (oral) Henn A K-03 (oral) Hermine O P-10 (poster) Herve G H-11 (poster)

Hillon P P-10 (poster) Hinds **B** M-06 (oral) Hines LE J-01 (oral) Hiorai Y F-09 (oral) His ED K-02 (oral) Ho J P-01 (oral) Hodak E A-05 (oral) A-06 (oral) C-01 (oral) C-02 (oral) C-03 (oral) H-06 (poster) K-05 (oral) M-09 (oral) P-06 (oral) Hoetzenecker W E-08 (oral) Hong EK O-05 (oral) Honig B M-12 (oral) Hoot JW P-01 (oral) Hoppe RT C-01 (oral) C-03 (oral) O-05 (oral) Horita A P-08 (poster) Horowitz D O-05 (oral) Horstein N M-12 (oral) Horton B C-04 (oral) Horwitz SM C-01 (oral) C-03 (oral) J-09 (poster) K-02 (oral) L-04 (oral) O-01 (oral) O-10 (oral) Huang Y O-09 (oral)

Hummel M B-05 (oral) F-06 (oral) Hurabielle C F-05 (oral) I-04 (oral) Huwe J J-05 (oral) Hwang S E-10 (oral) Hymes KB G-04 (oral) Ibrahim MA F-10 (poster) Ignatova D E-08 (oral) Illidge T K-07 (poster) Inclan-Alarcon S I-04 (oral) Ingen-Housz-Oro S H-11 (poster) K-03 (oral) Inozume T F-01 (oral) Irwin C N-04 (oral) Israeli M A-06 (oral) Ivan D A-02 (oral) Ivanov P E-08 (oral) Iversen L K-04 (oral) Iwatsuki K F-08 (oral) F-09 (oral) Jackson AL M-02 (oral) Jacob-Hirsch J A-05 (oral) Jain K B-07 (oral) Jamieson L K-07 (poster) Janin A O-02 (oral) Jansen PM I-02 (oral) I-03 (oral) Jariwala N

E-05 (oral) Jeskanen L F-07 (oral) Jirau Serrano XO M-12 (oral) John S G-01 (oral) Joly P O-06 (oral) Jonak C C-02 (oral) C-03 (oral) H-08 (poster) J-04 (oral) J-07 (poster) N-07 (poster) Jumaa H H-01 (oral) Junkins-Hopkins J A-02 (oral) Just U N-07 (poster) Kadin ME F-07 (oral) I-01 (oral) M-03 (oral) Kaminiski M G-10 (poster) Kannan K G-04 (oral) Kantor RW A-04 (oral) Kaplan J K-01 (oral) Kaplan MH G-10 (poster) Karakitsos P M-11 (oral) Karambidou K A-07 (poster) Katan M B-03 (oral) Kawaguchi M F-01 (oral) Kempf W C-02 (oral) C-04 (oral) E-09 (oral) H-03 (oral) Kerl K E-08 (oral) H-03 (oral)

Khatami R P-11 (poster) Kheterpal M C-03 (oral) J-09 (poster) L-04 (oral) Kho T P-01 (oral) Khodadoust MS O-03 (oral) O-05 (oral) O-10 (oral) O-11 (poster) **Kielbasa SM** H-01 (oral) Kiely C K-09 (poster) Kim BS E-05 (oral) Kim EJ A-02 (oral) C-03 (oral) J-03 (oral) N-09 (poster) P-03 (oral) Kim J A-02 (oral) C-04 (oral) F-03 (oral) O-10 (oral) Kim YH A-02 (oral) C-01 (oral) C-02 (oral) C-03 (oral) C-04 (oral) F-03 (oral) O-01 (oral) O-03 (oral) O-04 (oral) O-05 (oral) O-10 (oral) O-11 (poster) Kirsch I G-05 (oral) Kirsch IR G-06 (oral) Kittipongdaja W B-08 (oral) Klapper W F-04 (oral) Knobler R

C-02 (oral) C-03 (oral) J-04 (oral) N-07 (poster) Ko J P-19 (poster) Koens L H-01 (oral) Koguchi A P-13 (poster) Koh HY D-06 (poster) Koh MJ D-06 (poster) D-07 (poster) Kohler C F-04 (oral) Kohrt HE O-10 (oral) Koletsa T C-02 (oral) Koning MT H-01 (oral) H-02 (oral) Kontsioti F M-11 (oral) Koralov SB G-04 (oral) Kossenkov AV E-05 (oral) Kouloulias V P-02 (oral) Kraft A P-10 (poster) Krammer PH M-01 (oral) Kronthaler K M-10 (oral) Krueger JG G-06 (oral) Kuciejewska A K-09 (poster) N-04 (oral) Kupper TS G-02 (oral) G-05 (oral) G-06 (oral) Kurokawa M P-13 (poster) Kutok J G-04 (oral)

O-04 (oral) Lackey J O-09 (oral) Lam M M-04 (oral) Lamm Vb P-01 (oral) Lamoureux A H-09 (poster) Landry DW M-12 (oral) Lange M E-11 (poster) Langridge T N-08 (poster) Lansigan F K-02 (oral) N-13 (poster) Lares A O-05 (oral) Laroche L H-07 (poster) K-03 (oral) P-10 (poster) P-18 (poster) Latkowski J G-04 (oral) Laturnus M F-06 (oral) Lawrence C O-05 (oral) Lawson C P-17 (poster) Leahy P M-04 (oral) Lebbé C I-05 (oral) Leblanc R N-13 (poster) Leboeuf C O-02 (oral) LeBoeuf NR G-02 (oral) G-06 (oral) Lebowitz E J-09 (poster) Leclec'h C H-11 (poster) Leclerc-Mercier S P-10 (poster) Lee HY D-06 (poster)

Kuzel TM

Lee MW D-01 (oral) K-06 (poster) Lee WJ D-01 (oral) K-06 (poster) Lehner-Baumgartner E J-04 (oral) Lentzsch S M-12 (oral) Lenze D B-05 (oral) F-06 (oral) Lermontov S N-06 (poster) Levy A H-07 (poster) P-18 (poster) Lewis H J-08 (poster) Lewis J G-03 (oral) Li K F-11 (poster) Li S F-03 (oral) M-12 (oral) O-01 (oral) O-10 (oral) Lindahl LM K-04 (oral) Lipkin WI B-07 (oral) Lipner C J-05 (oral) Lipsanen T F-07 (oral) Lipstein MM M-12 (oral) Liszewski W L-01 (oral) Liu C G-04 (oral) Lome-Maldonado C I-04 (oral) López Guillermo A I-08 (poster) Lowry EL G-02 (oral) G-05 (oral) G-06 (oral) Luigia V

P-16 (poster) Machado JRS N-06 (poster) Machet L H-11 (poster) Maecker H O-10 (oral) Maeda M M-03 (oral) Maillard A O-06 (oral) Maiorana-Boutilier AL M-08 (oral) Maity A O-05 (oral) Malek M E-11 (poster) Maliniemi P F-07 (oral) Mallet V P-10 (poster) Malone DC J-01 (oral) Manfrere K E-04 (oral) E-07 (oral) Mangold AR C-04 (oral) K-05 (oral) Mangone MA M-12 (oral) Marc S H-07 (poster) Marie-Cardine A F-05 (oral) O-03 (oral) O-06 (poster) Marinho E K-03 (oral) Marinos L A-07 (poster) C-02 (oral) Markovitz D G-10 (poster) Maroñas-Jiménez L O-08 (oral) Marschalko M C-02 (oral) Marshall WS M-02 (oral) Martin-Clavijo A J-08 (poster)

Martinez F H-04 (oral) Martinez-Escala ME A-02 (oral) A-04 (oral) C-03 (oral) H-10 (poster) K-01 (oral) Maskin M D-05 (poster) P-07 (poster) Mathas S F-06 (oral) Mathieu S N-05 (oral) O-03 (oral) O-11 (poster) P-04 (oral) Maubec E H-07 (poster) K-03 (oral) O-06 (oral) P-18 (poster) Maule M C-03 (oral) Maurier N M-01 (oral) Maurus K L-02 (oral) McCaffrey S J-02 (oral) McCalmont TH M-06 (oral) McCann S J-05 (oral) O-07 (oral) McCormack C C-03 (oral) McCormick T M-04 (oral) McHargue C P-19 (poster) Mcormick G K-09 (poster) Meignin V I-05 (oral) Meiss R D-05 (poster) Melhem-Bertrandt A O-09 (oral) Menasce L K-07 (poster)

Menezes RF N-06 (poster) Menguy S H-04 (oral) Merlio JP H-04 (oral) I-07 (oral) O-06 (oral) Merlo V A-03 (oral) Merlo VI I-06 (oral) Mermin D O-06 (oral) Mertz K H-03 (oral) Michel L F-02 (oral) K-03 (oral) Milpied N H-09 (poster) **Misailovic S** E-08 (oral) Mitchell TJ B-03 (oral) G-01 (oral) G-09 (poster) Mitteldorf C C-02 (oral) H-03 (oral) Miura M F-08 (oral) Miyagaki T C-03 (oral) F-01 (oral) P-13 (poster) Miyake A P-08 (poster) Miyake T F-09 (oral) Miyashiro D C-03 (oral) D-02 (oral) E-04 (oral) E-07 (oral) L-03 (oral) Möbs M B-05 (oral) F-06 (oral) M-01 (oral) Mody K O-04 (oral)

Mohammad S G-10 (poster) Montante-Montes de Oca D Nagy-Szakal D I-04 (oral) Moon IJ D-01 (oral) K-06 (poster) Mori WS J-06 (poster) Morishita K F-08 (oral) Morris SL C-02 (oral) K-09 (poster) N-04 (oral) Mortier L O-06 (oral) Moskowitz A J-09 (poster) L-04 (oral) O-10 (oral) Mosquera NC G-01 (oral) Moss P G-08 (oral) Moss PAH E-12 (poster) Motta B N-01 (oral) N-10 (poster) Motta L K-07 (poster) Moyal L A-05 (oral) M-09 (oral) Mozas P I-08 (poster) Müller-Decker K M-01 (oral) Muniesa C C-02 (oral) C-03 (oral) O-08 (oral) Murray DJ E-12 (poster) G-08 (oral) N-11 (poster) Musiek A P-19 (poster) Myskowski PL J-09 (poster) L-04 (oral)

Nagao M J-02 (oral) B-07 (oral) Najidh S F-02 (oral) Nakagawa M M-03 (oral) Nakamura K P-13 (poster) Narbaitz M D-05 (poster) Narendran V G-04 (oral) Nasta SD N-09 (poster) Naym DG L-01 (oral) Ni X N-08 (poster) Nicola L P-07 (poster) Nicolay JP M-01 (oral) Nikolaou V A-07 (poster) C-02 (oral) C-03 (oral) P-02 (oral) Nowicki R E-11 (poster) Noyvert B G-08 (oral) Nudelman A M-09 (oral) O'Connor OA M-12 (oral) O-09 (oral) O'Malley JT G-05 (oral) G-06 (oral) O'Malley JT G-02 (oral) Ødum N G-04 (oral) Oefner PJ F-07 (oral) Oetjen LK E-05 (oral) Ognibene G C-03 (oral) Ohmatsu H

P-08 (poster) Ohshima K F-08 (oral) Oka T F-01 (oral) Oksenhendler E I-05 (oral) Oliveira LM E-04 (oral) E-07 (oral) Olsen E A-02 (oral) C-01 (oral) Olszewska B E-11 (poster) Onida F A-03 (oral) C-03 (oral) N-01 (oral) N-10 (poster) Ooi C O-04 (oral) Oro S I-07 (oral) N-05 (oral) O-06 (oral) P-04 (oral) Ortiz-Romero PL C-02 (oral) C-03 (oral) O-08 (oral) Ortonne N H-11 (poster) I-07 (oral) K-03 (oral) Oschlies I F-04 (oral) Osman WM F-10 (poster) **Oyetakin-White P** M-04 (oral) Paiva C O-03 (oral) O-11 (poster) Palmer J E-01 (oral) Palomero T G-07 (oral) M-07 (oral) Pang SM D-06 (poster) Paniec P

H-08 (poster) Papadavid E A-07 (poster) C-02 (oral) C-03 (oral) M-11 (oral) P-02 (oral) Papageorgiou S M-11 (oral) Pappa V M-11 (oral) Parker T N-03 (oral) Parrens M I-07 (oral) Parry E K-07 (poster) Patatoukas G P-02 (oral) Patel VM B-03 (oral) Patrizi A E-06 (oral) Patrone CC G-07 (oral) M-07 (oral) O-05 (oral) Patsatsi A C-02 (oral) Paturel C O-11 (poster) Pavlovsky L A-06 (oral) P-06 (oral) Pawade J C-04 (oral) Peaks MS M-08 (oral) Pearce H E-12 (poster) Peffault de Latour R I-05 (oral) Pereira J D-02 (oral) Perera LP M-03 (oral) Perera PY M-03 (oral) Perez RP O-09 (oral) Pestano LA M-02 (oral)

Petrella T H-04 (oral) H-11 (poster) Petrus MN M-03 (oral) Pfaltz M H-03 (oral) Pham-Ledard A C-02 (oral) H-04 (oral) O-06 (oral) Phillips CM M-08 (oral) Pileri A C-03 (oral) E-06 (oral) P-22 (poster) Pilz K O-03 (oral) O-11 (poster) Pimpinelli N C-02 (oral) C-03 (oral) E-06 (oral) P-22 (poster) Pincus L A-02 (oral) C-04 (oral) M-05 (oral) M-06 (oral) Pinter-Brown LC K-02 (oral) Piris MA O-08 (oral) Pittelkow MR K-05 (oral) Platoni K P-02 (oral) Pol S P-10 (poster) Poligone B L-06 (oral) Pomerantz A I-04 (oral) Porcu P C-01 (oral) C-03 (oral) C-04 (oral) O-03 (oral) O-10 (oral) O-11 (poster) Porkert S

C-02 (oral) C-03 (oral) H-08 (poster) J-04 (oral) J-07 (poster) N-07 (poster) Posligua AL K-01 (oral) Postigo C O-08 (oral) Postigo-Llorente C C-03 (oral) Prag-Naveh H P-06 (oral) Prince HM C-01 (oral) C-03 (oral) O-04 (oral) Pro B K-01 (oral) K-02 (oral) Profanter R E-08 (oral) Przybylski G H-01 (oral) Pujals A I-07 (oral) Pujol RM B-06 (oral) K-05 (oral) Pulitzer M A-02 (oral) C-04 (oral) J-09 (poster) L-04 (oral) Quaglino P C-01 (oral) C-02 (oral) C-03 (oral) Quéreux G N-05 (oral) O-06 (oral) P-04 (oral) Querfeld C C-04 (oral) E-01 (oral) Raffoux E I-05 (oral) Rahbar Z F-03 (oral) O-01 (oral) O-10 (oral)

Ram-Wolff C C-02 (oral) C-03 (oral) F-05 (oral) I-05 (oral) N-05 (oral) O-02 (oral) O-03 (oral) O-06 (oral) O-11 (poster) P-04 (oral) Ranki A F-07 (oral) Reiter O A-06 (oral) Ren M O-04 (oral) Rengarajan B J-03 (oral) Rephaeli A M-09 (oral) Reyderman L O-04 (oral) Reyno LM O-09 (oral) Richardson C L-06 (oral) **Riedl E** J-04 (oral) **Rigopoulos D** M-11 (oral) P-02 (oral) Riveiro-Falkenbach E O-08 (oral) Rivet J I-05 (oral) Roberts K N-02 (oral) **Robins H** G-02 (oral) G-05 (oral) G-06 (oral) Robson A I-07 (oral) Rodman DM M-02 (oral) Rodríguez Peralto JL O-08 (oral) Rodríguez-Rodríguez S I-04 (oral) **Rogers K** C-03 (oral)

C-04 (oral) Rook AH C-03 (oral) E-05 (oral) G-05 (oral) N-09 (poster) O-05 (oral) O-10 (oral) Roque AM P-10 (poster) Rosen ST E-01 (oral) K-02 (oral) Rosenwald A L-02 (oral) Rosman I P-19 (poster) Rotem C A-05 (oral) M-09 (oral) Roth S L-02 (oral) Roulot D P-10 (poster) Rovira M I-08 (poster) Russo I P-14 (poster) Sable K A-02 (oral) Sable KA K-01 (oral) Sagher E P-12 (poster) Saito I P-08 (poster) Sakai-Valente NY L-03 (oral) Salam A K-09 (poster) Sallam MA F-10 (poster) Salva KA B-01 (oral) San Martín O O-08 (oral) Sanches JA C-03 (oral) D-02 (oral) E-04 (oral) E-07 (oral) L-03 (oral)

Sanchez JA N-06 (poster) Sánchez-Beato M O-08 (oral) Sanchez-Martin M M-07 (oral) Sandoval J B-06 (oral) Saporiti G N-01 (oral) N-10 (poster) Sato MN E-04 (oral) E-07 (oral) Sato S F-01 (oral) P-13 (poster) Savage KJ O-09 (oral) Sawas A O-09 (oral) Scaeffer A P-19 (poster) Scarisbrick JJ C-02 (oral) C-03 (oral) C-04 (oral) E-12 (poster) G-08 (oral) H-05 (oral) J-08 (poster) N-04 (oral) N-11 (poster) Schaffer A C-04 (oral) Schieke SM B-08 (oral) Schlaak M N-12 (poster) Schmidt CA H-01 (oral) Schmidt M K-04 (oral) Schrader AM I-02 (oral) Schrepfer S M-10 (oral) Schroeder A M-01 (oral) Schwartz M K-02 (oral) Scott LL

G-06 (oral) Scotto L M-12 (oral) Selim M A-02 (oral) Selph J M-04 (oral) Sepassi M J-02 (oral) Seropian S N-02 (oral) Servitje O B-06 (oral) C-02 (oral) C-03 (oral) O-08 (oral) Seto AG M-02 (oral) Shah F G-08 (oral) H-05 (oral) J-08 (poster) N-11 (poster) Shaikh SR M-08 (oral) Shanbhag S O-10 (oral) Sharma G J-02 (oral) Sharma V J-01 (oral) Sharon E O-10 (oral) Shen X F-11 (poster) Shenjere P K-07 (poster) Sherman S A-05 (oral) Shewchuk BM M-08 (oral) Shi R F-11 (poster) Shimizu J P-13 (poster) Shine R O-10 (oral) Shinohara M C-04 (oral) Shirai K N-13 (poster) Shiue L

N-08 (poster) Showe LC E-05 (oral) Shustov AR K-02 (oral) O-10 (oral) Sicard H F-05 (oral) I-05 (oral) O-02 (oral) O-03 (oral) O-11 (poster) Sicre de Fontbrune F I-05 (oral) Silva MM N-06 (poster) Sims P M-12 (oral) Siqueira SA D-02 (oral) Skowron F N-05 (oral) Smith E K-07 (poster) Socié G I-05 (oral) Sokol L O-10 (oral) Sokołowska-Wojdyło M E-11 (poster) Song J E-01 (oral) Sørensen HT K-04 (oral) Sotto MN D-02 (oral) Soverini G N-01 (oral) N-10 (poster) Spaccarelli N N-09 (poster) Spathis A M-11 (oral) Spicknall KE N-14 (poster) Stadler R C-01 (oral) C-02 (oral) C-03 (oral) N-12 (poster) Stavroulaki G M-11 (oral)

Stearns D N-13 (poster) Steininger A B-05 (oral) Stenger-Petersen S J-03 (oral) Sterry W B-05 (oral) Stevens A C-03 (oral) G-08 (oral) H-05 (oral) J-08 (poster) N-11 (poster) Stevens E P-12 (poster) Stockton J G-08 (oral) Stolz DB E-03 (oral) Stranzenbach R C-02 (oral) C-03 (oral) N-12 (poster) Stratigos A A-07 (poster) Subrahmanyam PB O-10 (oral) Subtil A A-02 (oral) Suga H F-01 (oral) Sugaya M C-03 (oral) F-01 (oral) F-08 (oral) P-13 (poster) Suggs A M-04 (oral) Sun A G-04 (oral) Sundram U F-03 (oral) Sundrud MS G-04 (oral) Szuhai K I-03 (oral) Tacastacas J M-04 (oral) Tagliaferri E N-01 (oral) N-10 (poster)

Takahashi K P-08 (poster) Takahashi N F-01 (oral) P-13 (poster) Takeshita J E-05 (oral) Takimoto S P-08 (poster) Tal E M-09 (oral) Talpur R C-03 (oral) O-01 (oral) Taoka K P-13 (poster) Tarasenko N M-09 (oral) Tasidou A A-07 (poster) Tatonetti NP M-12 (oral) **Teague JE** G-02 (oral) G-05 (oral) G-06 (oral) Tejasvi T G-10 (poster) P-12 (poster) Templier I O-06 (oral) Tensen CP E-02 (oral) F-02 (oral) H-01 (oral) H-02 (oral) I-03 (oral) Tetzlaff M A-02 (oral) C-04 (oral) Tetzlaff MT M-02 (oral) Thompson A K-05 (oral) Thonnart N F-05 (oral) O-11 (poster) Tomasini C C-02 (oral) Torrealba MP E-04 (oral) E-07 (oral)

Torres N D-05 (poster) Townson SM O-10 (oral) Trautinger F C-02 (oral) Trave F O-09 (oral) Trila C P-07 (poster) Tronnier M H-03 (oral) Tsuji S P-13 (poster) Turner D C-02 (oral) Übelhart R H-01 (oral) Ueda J P-13 (poster) Ullmann R B-05 (oral) Urwin R K-09 (poster) Vainstein V O-05 (oral) Väkevä L F-07 (oral) Valencak J H-08 (poster) J-07 (poster) Valentina M P-16 (poster) van der Zeeuw SA H-01 (oral) H-02 (oral) Van Horn JA P-21 (poster) van Santen S P-05 (oral) Vandersee S B-05 (oral) Vanzuli S D-05 (poster) Vaqué JP O-08 (oral) Vasconcelos R L-03 (oral) Vasilatou D M-11 (oral) Vechev M E-08 (oral)

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