



INSIDE THIS ISSUE

From the President and the Chief Executive Officer 2

Epigenetics & Biology of Cutaneous T-cell Lymphomas..... 4

Skincare Corner Q&A..... 6

Upcoming Events..... 8

Scientific Conference Highlights.... 10

Finding a Miracle the Hard Way: Barbara and Victor Bartolome..... 12

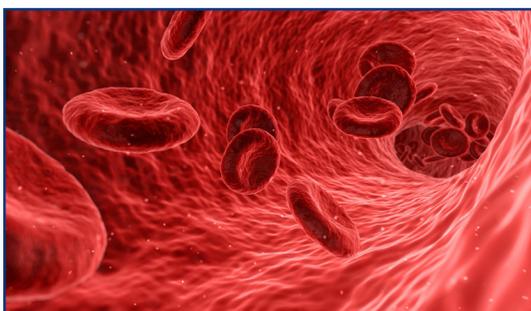
Making a Difference 15

THERAKOS / Mallinckrodt Pharmaceuticals Opportunity..... 15

Join us in Los Angeles..... 16

Modernizing Immunotherapy for CTCL

For decades, immunotherapy has been a cornerstone of systemic therapy for cutaneous T cell lymphoma (CTCL). Commonly used therapies, such as interferon, retinoids, and extracorporeal photopheresis (ECP), enhance anti-tumor immunity by activating some of the white blood cells that make up the body's own defenses against cancer.¹ It is therefore not surprising that modern immunotherapies, which target anti-tumor immunity in more sophisticated ways, have the potential to greatly improve our treatments for CTCL.



Inhibition of the programmed death-1 (PD-1) pathway, often called immune checkpoint inhibition, is one of the most successful strategies for inducing anti-tumor immunity in many types of cancer. However, until recently there was very little data for its use in CTCL.

In types of CTCL, like mycosis fungoides (MF) and Sézary syndrome (SS), molecules (ligands) that attach to PD-1, called PD-L1, are widely present on either cancer cells or normal white blood cells that are around the cancer cells. This suggests that the PD-1 pathway is one way the cancer cells hide from or block the body's immune system.² A phase II study led by the Cancer Immunotherapy Trials Network (CITN) evaluating pembrolizumab, an antibody to PD-1, showed promising results in people with higher stages of or relapsed MF and SS.³ In this study, 24 people were treated and 38% had at least 50% improvement in their lymphoma. Furthermore, many of these people experienced long term and ongoing benefit from treatment. Based upon these results, pembrolizumab is now listed in national guidelines as a treatment option for CTCL treatment and future studies combining pembrolizumab with other immune therapies are planned.

Another drug that was recently added to our armamentarium for CTCL is brentuximab vedotin (BV). BV is a drug with 2 parts – an antibody and chemotherapy, which are bound together. The antibody is designed to bind to a protein called CD30, which is often found on the surface of CTCL cells. When BV binds to CD30-positive tumor cells, it enters and kills the cells through the action of the chemotherapy.⁴ BV was recently evaluated in people with MF in a phase III study in

Authored by:

Steven Horwitz, MD
Memorial Sloan-Kettering Cancer Center
New York, NY

Youn Kim, MD
Stanford Cancer Center
Palo Alto, CA

Alison Moskowitz, MD
Memorial Sloan-Kettering Cancer Center
New York, NY

Cutaneous Lymphoma Foundation
PO Box 374
Birmingham, MI 48012-0374
telephone: (248) 644-9014
fax: (248) 644-9014
email: info@clfoundation.org
www.clfoundation.org

Forum is published by the Cutaneous Lymphoma Foundation.
Editor: Hilary Romkey
Layout & Design: Bridget Safadi

Disclaimer

The Cutaneous Lymphoma Foundation does not endorse any drugs, treatments or products reported in this newsletter. Information is provided for informational purposes only. Because the symptoms and severity of cutaneous lymphoma vary among individuals, the Cutaneous Lymphoma Foundation recommends that all drugs and treatments be discussed with the reader's physician(s) for proper evaluation, treatment and medical care.

From the Chief Executive Officer



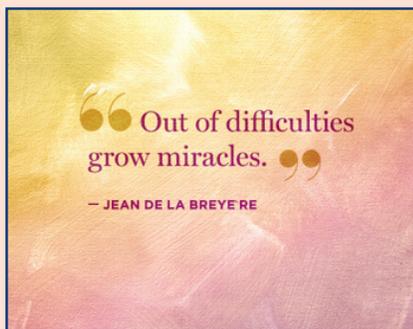
Susan Thornton

As usual, this edition of the Forum focuses on research and updates from the latest round of medical meetings. The last six months have been overflowing with scientific and clinical data

about cutaneous lymphoma. To be quite honest, the research that has been going on is mind boggling.

This year was special; the 3rd World Congress of Cutaneous Lymphomas was held in New York City in October. As the name implies, this is only the third time a scientific, research, and clinical conference has been convened specifically in the area of cutaneous lymphoma.

There were over 400 people in attendance from around the globe, all dedicated to the quest for answers about this group of rare lymphomas. It was an extraordinary



program where all areas of research were presented and discussed. Everything from bench to bedside was shared. This conference was followed in January by the annual T-Cell Forum and the annual United States Cutaneous Lymphoma Consortium Workshop in March.

The big takeaway is that there is still so much to learn. Why does the disease occur? What is different and the same about the various subtypes? What targets and markers should be focused on when diagnosing? How can you tell if a treatment is working? What are the best treatments over the course of time for which person? What new targets are promising? Can there be treatments developed for those targets? What is currently in the clinical trial pipeline? Are there other new approaches to combining current treatments for better outcomes? All these questions are being asked and often answered. I personally came away from these programs with a new sense of hope that what is being revealed through the research will have a huge impact on all of us living with cutaneous lymphoma in the not too distant future.

From the CEO...continued on page 7

From the President



Joe Eischens

Hello again, and happy Spring to all of you! If you are like me, you are looking forward to getting some real sun; not just for healing purposes, but also for the energy boost and good feelings we get from some warm sunshine! Always a welcome change.

Speaking of welcome changes, soon you will all be the beneficiaries of newly revamped Cutaneous Lymphoma Foundation (CLF) website, thanks to the hard work and dedication of the CLF staff! We hope you'll be pleasantly surprised by how easy it will be to navigate our new website. In addition, it will still have a wealth of information and resources, including touching personal stories, a comprehensive database of providers and health centers, and the largest compilation of relevant research you can find anywhere on the web for cutaneous lymphomas and its varied forms. We are very excited about these changes and hope you will be too. Please let us know what you think about the revamped website when it is released.

I also want to give a much deserved "thank you" to the wonderful staff and team of researchers we have working for and with the Foundation. Many of you recently received our annual research report and I cannot tell you how proud and excited I am about the tremendous work so many are doing to help all of us in our daily struggles with cutaneous lymphomas. The report simply highlights the important research our dedicated and intelligent (and humble) team of medical professionals are conducting every day. All done with the goal of easing our pain and giving us all tremendous hope that one day we can all be free of the cutaneous lymphoma shackles. Please take a moment to review this outstanding research.

By the way, "Research" is the timely topic of this newsletter. In these pages you will find the most recent update on the research currently being conducted, an informative description of the pathology, epigenetics and biology of CTCL, and the always-appreciated skincare tips. Of course, we hope our website, along with these newsletters and other mailings you receive from us will compel you to attend one of our numerous Patient Education Forums and Ask the Experts events that take

From the President...continued on page 7

Forum

The newsletter of the Cutaneous Lymphoma Foundation
ALL RIGHTS RESERVED

*Cutaneous Lymphoma Foundation is a 501(c)(3) non-profit organization.
Donations are tax deductible to the extent allowed by law.*

BOARD OF DIRECTORS

OFFICERS

Joe Eischens, Esq.	President
Marianne Tawa	Vice President
Jeff Ward	Treasurer
Laurel Carlson	Secretary

DIRECTORS

Steven Horwitz, MD	Director
Youn Kim, MD	Director
Lauren Pinter-Brown, MD	Director
Mike Silver	Director
Michael W. Young	Director
Susan Thornton	Chief Executive Officer

RESEARCH ADVISORY COUNCIL

Pierluigi Porcu, MD	Chair
---------------------	-------

SCIENTIFIC REVIEW COUNCIL

Stuart Lessin, MD	Chair
-------------------	-------

MEDICAL ADVISORY COUNCIL

Ellen Kim, MD, Chair	Penn Medicine
Thomas Anderson, MD	University of Michigan
Kevin Cooper, MD	Case Western Reserve University
Madeleine Duvic, MD	MD Anderson Cancer Center
Francine Foss, MD	Yale University School of Medicine
Lars French, MD	Geneva Medical Center
Sam Hwang, MD, PhD	The Medical College of Wisconsin
Robert Knobler, MD	University of Vienna
Thomas Kupper, MD	Brigham and Women's Hospital
Liliane Laroche, MD	University of Paris
Sue McCann, MSN, RN	University of Pittsburgh Medical Center
Lauren Pinter-Brown, MD	UC Irvine Health
David Ramsay, MD	New York University
Alain Rook, MD	University of Pennsylvania
Steven T. Rosen, MD	City of Hope
Martin Weinstock, MD, PhD	Brown University
Sean Whittaker, MD, MRCP	Guys & St. Thomas Hospital
Lynn Wilson, MD, MPH	Yale University School of Medicine

STAFF

Holly Priebe	Chief Operating and Financial Officer
Hilary Romkey	Program Manager
Tina Collins	Community Development Manager
Deb Van Zegeren	Administrative & Communications Manager
Bridget Safadi	Administrative Assistant



Find us on
Facebook

Check out the latest news and
information from the
Cutaneous Lymphoma Foundation
by liking us on Facebook!

What Is Cutaneous Lymphoma?

Cutaneous lymphomas are cancers of lymphocytes (white blood cells) that primarily involve the skin. Classification is based on lymphocyte type: B-lymphocytes (B-cell) or T-lymphocytes (T-cell). Cutaneous T-cell lymphoma (CTCL) is the most common type of cutaneous lymphoma that typically presents with red, scaly patches or thickened plaques of skin that often mimic eczema or chronic dermatitis. Progression from limited skin involvement is variable and may be accompanied by tumor formation, ulceration and exfoliation, complicated by itching and infections. Advanced stages are defined by involvement of lymph nodes, peripheral blood, and internal organs. 🦋

The Cutaneous Lymphoma Foundation's patient educational newsletter, **Forum**, has been made possible thanks to the following generous supporters:



ACTELION



GALDERMA



Mallinckrodt
Pharmaceuticals



VALEANT
Dermatology

Epigenetics & Biology of Cutaneous T-cell Lymphomas

Cutaneous T-cell Lymphomas (CTCL) are a family of extranodal T-cell non-Hodgkin's lymphomas (NHL) affecting primarily the skin that derive from skin-homing mature T-cells. While the skin is the main site of disease, CTCL are a type of blood cancer. The most common type of CTCL is mycosis fungoides (MF), which represents approximately 70% of all CTCL. In approximately two thirds of the cases, MF presents with early stage disease (stage IIA or less), causes a flat, scaly, rash, and has an indolent clinical course, with good prognosis. However, in



a significant fraction of patients, after a variable interval from diagnosis, the disease progresses to advanced stage (stage IIB or greater), with

tumor lesions in the skin, extracutaneous dissemination (blood, lymph nodes, visceral organs), and large cell transformation (LCT), all of which are associated with a worse prognosis. Patients with Sézary syndrome (SS) represent a very small but distinct subset of advanced stage CTCL, with extensive blood involvement. SS may arise de novo (i.e. from the onset) or evolve from pre-existent MF.

What triggers the development of MF, drives its progression from early to advanced stage, leads to the development of SS, and determines its sensitivity or resistance to the treatments available in the clinic has remained for a long time a mystery. However, over the past 2 years, a number of breakthrough molecular genetic studies have been published by several research groups worldwide that begin to shed some light on these critical aspects of the disease, and offer guidance for additional studies focused on new therapies that are likely to change its natural history, and positively impact patients' lives.¹⁻⁷

Most of these studies have focused on patients with advanced stage MF and SS thus offering an important but relatively narrow view of the abnormal molecular landscape of

these lymphomas. In aggregate, these studies provide valuable insight on the spectrum and the frequency of the mutations that accumulate in the tumor cell's DNA over the long trek from early onset, limited-stage disease, all the way to advanced stage, treatment-resistant, poor-risk disease. Many of these mutations no doubt represent

"background noise" or genomic "wear and tear", and some reflect the expected DNA damage resulting from life-long exposure of the skin to sunlight. Separating the wheat from the chaff - a task not always easy - is obviously a crucial part of this work. Some mutations, however, appear to affect parts of the cancer cell genome that contain bona fide or candidate "driver" cancer genes, that is genes that, once mutated, drive - or initiate - the cancer process. These are the genes that, once clearly identified, are expected to produce "dividends" in our search for a cure.

Some driver genes are the target of so-called gain-of-function (GOF) mutations. These are genes that stimulate normal cells' growth and replication when expressed at

the right time and in the right place. GOF mutations cause these genes to be switched into a constitutive "on" status. So altered, they are no longer responsive to physiologic feedback control loops and consequently cannot be turned "off". Other genes become "drivers" by loss-of-function (LOF) mutations. These are cellular genes that normally repress abnormal cell growth, and when mutated or deleted can no longer exert their physiologic function, leading to uncontrolled cell proliferation. While the precise hierarchy of driver genes and mutations in different cancers - including CTCL - remains to be defined, the knowledge gained from these studies is already being used to develop and test new drugs, and drug combinations, in clinical trials.

Authored by:

Pierluigi Porcu, MD
Sidney Kimmel Cancer
Center
Philadelphia, PA

Anjali Mishra, PhD
Ohio State University
Comprehensive Cancer
Center
Columbus, OH

"... over the past 2 years, a number of breakthrough molecular genetic studies have been published by several research groups worldwide..."

The mutational landscape analysis provided by these studies, however, is not informative about the early events leading to the initial development of CTCL, which occur years, possibly decades before progression to advanced stage disease. To gain some insight on the early mechanisms that trigger the development of CTCL and determine how they lead to disease progression, the best tools we currently have are spontaneous animal models of CTCL. By creating a genetically engineered mouse that constitutively produces large amounts of interleukin 15 (IL-15), a regulator of T-cell growth that is overexpressed in CTCL patients, our group was able to demonstrate that within 4-6 weeks of life, the IL-15 mice start to develop a T-cell lymphoma that replicates most of the features of human CTCL, including classical findings on skin biopsy, severe itching, and development of tumor lesions.⁸ Treatment of the IL-15 mice with drugs approved for human CTCL (romidepsin, vorinostat) within 4-6 weeks stops disease progression, whereas all mice treated with placebo die.⁸

How does IL-15 produce CTCL in mice? Our studies show that constant exposure of normal T-cells to IL-15 over time, leads to dramatic changes in the epigenetic control of thousands of genes, some of which belong to the same family of driver cancer genes that were found to be mutated in the CTCL genomic studies cited above. It is also of great interest that three of the genes that are highly overexpressed in CTCL as a consequence of chronic IL-15 exposure - histone deacetylase (HDAC) 1, HDAC2, and HDAC6 - are the primary target of romidepsin and vorinostat, suggesting a mechanism for the clinical efficacy of these drugs.⁹ HDAC1 and HDAC2, in turn, directly induce the expression of a well-known cancer-promoting gene called miR-21, which had been shown by several groups to be upregulated in CTCL. With more effective HDAC1 and HDAC2 inhibitors in clinical development,¹⁰ and with new drugs able to counteract the cancer-inducing effect of miR-21 on the horizon,¹¹ the possibility of a combined inhibition of these key CTCL-inducing genes will soon be a reality.



“... the possibility of a combined inhibition of these key CTCL-inducing genes will soon be a reality.”

Finally, what is the reason for the overproduction of IL-15 in CTCL patients? Using purified tumor samples, we were able to show that in CTCL patients ZEB1, an important negative regulator of IL-15, is prevented from exerting its normal function due to the aberrant DNA methylation of the control region (promoter) for the IL-15 gene.⁸ In the absence of the repressive effect of ZEB1, human T-cells start producing large amounts of IL-15, activating the same cancer-inducing pathways (HDAC1, HDAC2, miR-21) that we had carefully characterized in the IL-15 mice. These observations have important treatment implications because drugs that decrease DNA methylation may be able to restore ZEB1's physiologic repression of IL-15, thus interrupting this cancer signaling loop. The story comes full circle with the observation that many of the genomic CTCL studies cited above showed that ZEB1 was one of the most common cancer suppressor genes subject to LOF mutations, supporting its important role in the development of CTCL.

These are exciting times in CTCL research. The hard work of laboratory and clinical investigators worldwide is starting to bear fruit, and a number of basic discoveries in the genetic and epigenetic foundations of CTCL are now being translated into novel therapies, with great impact for patients.

References

1. Ungewickell A, Bhaduri A, Rios E, Reuter J, Lee CS, Mah A, Zehnder A, Ohgami R, Kulkarni S, Armstrong R, Weng WK, Gratzinger D, Tavallae M, Rook A, Snyder M, Kim Y, Khavari PA. Genomic analysis of mycosis fungoides and Sézary syndrome identifies recurrent alterations in TNFR2. *Nat Genet.* 2015 Sep;47(9):1056-60
2. Choi J, Goh G, Walradt T, Hong BS, Bunick CG, Chen K, Bjornson RD, Maman Y, Wang T, Tordoff J, Carlson K, Overton JD, Liu KJ, Lewis JM, Devine L, Barbarotta L, Foss FM, Subtil A, Vonderheid EC, Edelson RL, Schatz DG, Boggon TJ, Girardi M, Lifton RP. Genomic landscape of cutaneous T cell lymphoma. *Nat Genet.* 2015 Sep;47(9):1011-9
3. Wang L, Ni X, Covington KR, Yang BY, Shiu J, Zhang X, Xi L, Meng Q, Langridge T, Drummond J, Donehower LA, Doddapaneni H, Muzny DM, Gibbs RA, Wheeler DA, Duvic M. Genomic profiling of Sézary syndrome identifies alterations of key T cell signaling and differentiation genes. *Nat Genet.* 2015 Dec;47(12):1426-34.

SKINCARE CORNER Q&A

Question: *Do you recommend the use of cold compresses? If not, why not? If so, when and how? For what conditions? And lastly, is a cold compress the same as a wet wrap?*

Cold compresses can occasionally provide mild relief from bothersome itching and the inflammation that often accompanies it. The cold temperature offers a numbing effect on the targeted area and helps to decrease related swelling. As the effect is generally only temporary, I caution against the frequent or prolonged use of cold compresses as



a mainstay of a management regimen. It is important to protect the skin from direct contact with the compress and use a cloth barrier (like a towel) between the two. I also recommend that it not be applied for longer than 20 minutes at a time and allow at least 1 hour in between applications if a repeat is needed.

When applied in a conscientious manner, cold compresses are generally fairly safe to use for a variety of itch-provoking conditions. They are most reasonably employed when the itch is localized and not spread over large areas of the body. Patients suffering from itching related to more obvious sources such as bug

bites and sunburns often find relief from cold compresses. Additionally, itching related to conditions such as eczema, mycosis fungoides or psoriasis may also have some temporary benefit as well.

That is a great question! These are actually very different therapies. In a nutshell, wet wrapping is the process of creating a moisture barrier on the skin and then dressing the affected areas in damp wraps, followed by dry wraps. This can help relieve some itching by allowing the cream adequate time to penetrate the skin and also provides some cooling of the affected area as the water evaporates.

Answer provided by:

Allister Benjamin Chase, MSN, FNP-BC, AOCNP
Genentech
Los Angeles, CA

Our nerves are responsible for transmitting several sensations, including pain, itch, temperature, and pressure among others. While a lot remains to be understood about how our nerves and brain processes this information, we know that certain sensations, such as pain and itch, can be directly decreased with the use of hot or cold temperatures. Temperature can also indirectly affect the sensation of pain and itch by affecting blood flow, which affects local inflammation and swelling.

Cold compresses can take on many forms. A cold compress can be made from a homemade plastic bag filled with water and ice, a frozen bag of peas, an instant cold pack, or a cloth soaked with cold water. In general, a cold compress should not be left



on for more than 20 minutes at a time to prevent the development of frostbite.

Cold compresses are best used to suppress sensations of itch, a common problem in patients with cutaneous lymphoma. It can also help with certain types of pain, such as a sprained ankle or knee, where inflammation and swelling is contributing to pain. Interestingly, cooling agents, such as menthol (found in several over the counter creams like Sarna), can also decrease itching. The cold compress should be placed on the areas where the itch is most bothersome and can be rotated around to different parts of the body.

Wet wraps are different from cold compresses, as their goal is to increase the water content of skin. They involve wearing clothing (e.g. long pajamas) soaked first with warm water, often covered by another layer of dry clothing. They are proven effective in conditions with dry skin and itching, like eczema.

Using cool water may provide an even greater advantage for itch relief but as large parts of the body will be damp this may be more uncomfortable.

Patient with cutaneous lymphoma should consider use of cold compresses as well as wet wraps to reduce itch caused by their skin disease and dry skin, another common problem.



Use of hot compresses, or being in hot environments, tends to make itching worse by increasing blood flow, inflammation, and sweat, which can be an irritant to skin. This is why after a warm shower skin lesions of lymphoma can temporarily appear redder and may itch more. Only painfully hot temperatures can briefly decrease the sensation of itch, which is not recommended. Hot showers may seem a tempting solution to itching but this causes worsening dry skin and makes itching more challenging to manage afterwards. Hot compresses are best for helping with muscle cramps or on an infectious boil, abscess, or cyst where increased blood flow is desired to speed recovery.

Answer provided by:
Cecilia Larocca, MD
Dana-Farber/Brigham and Women's Cancer Center
Boston, MA

From the CEO...continued

If you want a great explanation about why all of this research is critical, take the time to watch the video captured at the 2-day Patient Program in New York of the presentations by Drs. Julia Scarisbrick and Maarten Vermeer available through the Online Learning Center. In my opinion, it is worth taking the 35 minutes to watch. It helps to make sense out of the complex science.

The bottom line is, it's complicated! However, the articles in this edition of the Forum will attempt to help you understand the science behind the research, why it's important and why you can be hopeful that all the work will result in something tangible that we, as patients, can take advantage of.

Enjoy the articles. After you have read the issue, you will have earned your Gold Star as a Citizen Scientist!

We look forward to seeing you at an upcoming live program or interacting with you along the way via email, phone or social media. Our doors, email and phone lines are always open.

Cheers,

From the President...continued

place all over the country. Please check the pages of this newsletter for the event nearest you, and if you get the opportunity to attend, please do! You won't be disappointed.

Finally, a great big shout out to all of our wonderful supporters, without whom we would be unable to bring you all of this wonderful research and information. If you find yourself with a few extra dollars in your pocket after tax season, please consider making a donation to the CLF so that we can continue to provide the services you need.

In recovery's good stead, I humbly thank all of you, and we here at the Foundation wish all the best to you.

Cutaneous Lymphoma Patient Educational Opportunities

The Cutaneous Lymphoma Foundation offers free Patient Educational Forums throughout North America providing an opportunity to:

- Receive the latest information about cutaneous lymphoma and learn about treatment options from experts in the field.
- Learn what's new in cutaneous lymphoma research and clinical trials.
- Q & A sessions - probably the most popular portion of the day. Have questions about the different types of cutaneous lymphoma, treatments, or daily living? The Q & A sessions provide you an opportunity to ask in a relaxed and friendly environment.
- Meet and network with other individuals affected by cutaneous lymphoma. Being diagnosed with or caring for an individual with a rare disease can be lonely. Meet others who know and understand what you are going through.
- Learn about available resources for treatment and support.

We hope to see you at an event soon!

Patient Networking Groups

The Cutaneous Lymphoma Foundation also offers monthly patient networking groups in the cities listed below. Visit our website for more details on meeting times and locations.

CLF-DC

Fairfax, Virginia

www.clfoundation.org/CLF-DC

CLR-LV

Las Vegas, Nevada

www.clfoundation.org/CLF-LV

CLF-NYC

New York, New York

www.clfoundation.org/CLF-NYC

CLF-OR

Portland, Oregon

www.clfoundation.org/CLF-OR

CLF-SLC

Salt Lake City, Utah

www.clfoundation.org/CLF-SLC

Upcoming 2017 Events*



May 13, 2017: Memphis, TN
Cutaneous Lymphoma Foundation
Patient Educational Forum



June 24 & 25 2017: Los Angeles, CA
Cutaneous Lymphoma Foundation
2-Day Patient Conference



September 30, 2017: Portland, OR
Cutaneous Lymphoma Foundation
Patient Educational Forum



October 4, 2017: Pittsburgh, PA
Cutaneous Lymphoma Foundation
Patient Educational Forum



November 11, 2017: Hackensack, NJ
Cutaneous Lymphoma Foundation
Answers from the Experts...Live!

For more information and to register for these events, visit www.clfoundation.org or call 248.644.9014, ext. 4.

** Dates and venues are subject to change. Please check the website for detailed information.*

The Cutaneous Lymphoma Foundation extends its thanks to the following generous supporters of our events:



Modernizing Immunotherapy for CTCL...continued

which it was compared to methotrexate or bexarotene. BV was much more effective in treating MF than either of the other drugs (response rate to BV was 65% compared to 10% for the other drugs). BV can cause side effects; most common of which is neuropathy, or numbness in fingers and toes, however it is typically well tolerated. Based upon its impressive activity in MF, BV is listed in national guidelines as a treatment option for CD30 positive MF.

A drug that is not yet FDA approved (but may become approved for MF and SS) is mogamulizumab, an antibody that binds to a protein called CCR4. CCR4 is present on both tumor cells and immune cells. As a result, mogamulizumab likely works by 2 mechanisms - it directly depletes tumor cells and enhances anti-tumor immunity. This drug was evaluated in 41 people with MF or SS and 37% experienced at least 50% reduction in their lymphoma.⁵ It was next evaluated in a randomized study (phase III) in which it was compared to vorinostat. The results from this phase III study are not yet available. However, if the study shows that mogamulizumab is more active than vorinostat for MF or SS, it could lead to its FDA approval for these diseases.

Additional immune therapies that show promising activity in MF and SS are currently being evaluated in clinical trials. One such drug is an antibody that binds to KIR3DL2, a protein present on CTCL tumor cells.⁶ Another interesting therapy is low dose skin radiation combined with an immune enhancer called IL-12.⁷ Both of these therapies are in early phases of study but have the potential to improve and broaden treatment options for CTCL.

Overall, immune therapy continues to play an important role in the treatment of CTCL. Newer immunotherapies, such as pembrolizumab and BV, are already available and additional therapies may be close to approval. Given the past success of more traditional immune-modulatory therapies in CTCL, these modern approaches are likely to significantly improve treatment options for people with MF and SS.

“Additional immune therapies that show promising activity in MF and SS are currently being evaluated in clinical trials.”

1. Kim EJ, Hess S, Richardson SK, Newton S, Showe LC, Benoit BM, Ubriani R, Vittorio CC, Junkins-Hopkins JM, Wysłocka M, Rook AH. Immunopathogenesis and therapy of cutaneous T cell lymphoma. *The Journal of clinical investigation* 2005;115:798-812.
2. Wilcox RA, Feldman AL, Wada DA, Yang ZZ, Comfere NI, Dong H, Kwon ED, Novak AJ, Markovic SN, Pittelkow MR, Witzig TE, Ansell SM. B7-H1 (PD-L1, CD274) suppresses host immunity in T-cell lymphoproliferative disorders. *Blood* 2009;114:2149-58.
3. Khodadoust M, Rook AH, Porcu P, Foss FM, Moskowitz AJ, Shustov AR, Shanbhag S, Sokol L, Shine R, Fling SP, Li S, Rabhar Z, Kim J, Yang Y, Yearley J, Chartash EK, Townson SM, Subrahmanyam PB, Maecker H, Alizadeh AA, Dai J, Horwitz SM, Sharon E, Kohrt H, Cheever MA, Kim Y. Pembrolizumab for Treatment of Relapsed/Refractory Mycosis Fungoides and Sézary Syndrome: Clinical Efficacy in a Citn Multicenter Phase 2 Study. 2016.
4. Kim YH, Whittaker S, Horwitz SM, Duvic M, Dummer R, Scarisbrick JJ, Quaglino P, Zinzani PL, Wolter P, Wang Y, Palanca-Wessels MC, Zagadailov E, Trepicchio WL, Liu Y, Little M, Prince HM. Brentuximab Vedotin Demonstrates Significantly Superior Clinical Outcomes in Patients with CD30-Expressing Cutaneous T Cell Lymphoma Versus Physician's Choice (Methotrexate or Bexarotene): The Phase 3 Alcanza Study. *ASH Annual Meeting Abstracts* 2016:Abstract 182.
5. Duvic M, Pinter-Brown LC, Foss FM, Sokol L, Jorgensen JL, Challagundla P, Dwyer KM, Zhang X, Kurman MR, Ballerini R, Liu L, Kim YH. Phase 1/2 study of mogamulizumab, a defucosylated anti-CCR4 antibody, in previously treated patients with cutaneous T-cell lymphoma. 2015.
6. Bagot M, Porcu P, Ram-Wolff C, Khodadoust M, Battistella M, Marie-Cardine A, Mathieu S, Vermeer MH, Whittaker S, Duvic M, Bensussan A, Paturel C, Bonnafous C, Thonnart N, Widemann A, Bonin C, Sicard H, Paiva C, Pilz K, Kim Y. First-in-Human, Multicenter Phase I Study of IPH4102, First-in-Class Humanized Anti-KIR3DL2 Monoclonal Antibody, in Relapsed/Refractory Cutaneous T-Cell Lymphomas: Preliminary Safety, Exploratory and Clinical Activity Results. 2016.
7. Duvic M, Sherman ML, Wood GS, Kuzel TM, Olsen E, Foss F, Laliberte RJ, Ryan JL, Zonno K, Rook AH. A phase II open-label study of recombinant human interleukin-12 in patients with stage IA, IB, or IIA mycosis fungoides. *Journal of the American Academy of Dermatology* 2006;55:807-13.

Scientific Conference Highlights

Beginning with the 3rd World Congress of Cutaneous Lymphomas, through the annual T-Cell Symposium, and the United States Cutaneous Lymphoma Consortium Workshop, exciting information has been shared among the clinical and scientific communities dedicated to understanding and discovery in cutaneous lymphoma.

A substantial amount of research and clinical work is going on around the world dedicated cutaneous lymphoma. As we hear often, cutaneous lymphoma is a complex disease. Researchers are just scratching the surface of understanding this complexity. As Dr. Michael Girardi shared during his presentation at the World Congress, “cutaneous lymphoma is a group of defects of the immune system. We need to work with the immune system, not against it”. T-cell biology is about checks and balances. Cutaneous lymphoma arises when these checks and balances are not working properly. Learning where these defects are, figuring out how to target therapy to correct what isn’t working and being able to monitor and manage the effectiveness of treatment quickly is the work being done to find effective treatments and hopefully, one day, eradicate this group of diseases.

The depth of content that was shared at these valuable conferences is too vast to include in one article. Below is a synopsis of each meeting; Susan’s full highlights are available in the Medical Meeting Highlights callout section on this webpage: www.clfoundation.org/medicalmeetings

3rd World Congress of Cutaneous Lymphomas October 26-28, 2016 - New York City, NY

This was this largest scientific and clinical gathering in the history of cutaneous lymphoma specific meetings. Over 400 participants from all over the world convened in New York to learn, share and discuss the data that has been collected to date. There were 160 abstract posters and over 100 oral presentations given over the course of the meeting. All areas of specialty were represented providing a broad spectrum of topics discussed ranging from genetics to applied bench research, therapeutics to clinical management and treatment developments.

After a welcome by the co-chairs of the meeting, Drs. Maarten Vermeer from the Netherlands and Larisa Geskin from the United States, the program began with Dr. Steven Swerdlow, Professor of Pathology and Director of the Division of Hematopathology at the University of Pittsburgh. Dr. Swerdlow presented the history of the World Health Organization classification of cutaneous lymphomas, sharing that the first global consensus of classifications in cutaneous lymphoma was published

in 2006. Updates and revisions continue to be made in collaboration with global clinical advisory committees. Why are these global disease classifications important? As the knowledge continues to deepen and grow about the variations of the different types of cutaneous lymphomas, the classifications continue to expand or be enhanced which provides clinicians a better framework for diagnosing and treating patients. Much progress has been made in the last several years, as was noted by the depth and breadth of presentations at this important meeting.

Highlights:

- The landscape of cutaneous lymphoma mutations are very complex. There are no single targets that will be the “silver bullet” to managing the disease or finding a cure. Much research is being done to understand the underlying changes that occur at the cellular level, where the immune system is not working properly and how different treatments are working in order to find the best single or combination treatments for the various subtypes of cutaneous lymphoma diseases.
- Some of these areas of focus are:
 - » JAK/Stat pathway - errors in the cell death signals
 - » Role of IL-13 signaling pathway
 - » KIR3DL2 is a recently discovered marker of the malignant clonal cell population in Sézary Syndrome
 - » PD-L1 expression in both cutaneous T-cell and cutaneous B-cell as a potential target for treatment using new drugs that target this error in the immune system
 - » Distinct separation of CD30+ lymphoproliferative disorders from other cutaneous lymphomas
 - » microRNA molecules that impact cutaneous lymphoma as potential treatment targets
 - » Many new clinical trials are underway or in the planning process including, but not limited to:
 - IPH4102-101 - targets KIR3DL2
 - MRG-106 - targeting miR-155-5p
 - E7777 - reformulated denliekin diftitox (original brand name of Ontak)
 - Low dose total skin electron beam (TSEB) in combination with NM-IL-12 which targets errors in this cell pathway that allows the cancerous T-cells to evade and escape programmed cell death
 - AG567E - which targets CD37 protein on the cancer cell surface

Epigenetics & Biology of Cutaneous T-cell Lymphomas ...continued

Presentations were given regarding the best method for determining when a stem cell transplant should be considered and the conditioning regimens that should be used. Specific case studies were shared that provided insights from different institutions on how to treat challenging disease that occurs in sanctuary areas of the body or aggressive disease using different combination therapies. Potential recommendations for future clinical trials of combination treatments were also discussed.

It was clear that it takes collaboration from all aspects of research to unravel the mysteries around cutaneous lymphoma. From the laboratory petri dish and mouse models, through to the clinic where the treating physician works with the patient to determine the best strategy for treatment, are all critical components to understanding this disease. The multidisciplinary approach to research is critical in moving forward in the understanding of how the disease functions so the appropriate focus can be put on those areas that will have the biggest impact on disease management and treatment.

This conference enabled clinicians and scientists to assess collectively the current state of cutaneous lymphoma, resulting in the development of new projects and ventures that leverage expertise around the world. The spirit of collaboration and excitement at the meeting was tangible. Everyone in attendance is committed to working together at all levels toward the shared goal of developing better understandings of these diseases, best treatment regimens, new therapeutic targets and a relentless focus on finding a cure.

T-Cell Lymphoma Forum - 9th Annual January 26-28, 2017 - San Francisco, CA

This scientific meeting occurs every January, bringing experts in T-cell lymphomas from around the world together to covers the entire landscape of T-cell malignancies, including peripheral T-cell lymphomas (PTCLs), cutaneous T-cell lymphomas (CTCL) and natural killer cell lymphomas (NK).

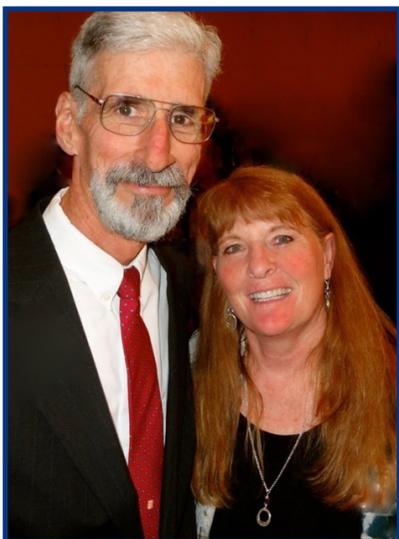
The keynote address, “What I know and don’t know about CTCL”, was presented by Dr. Madeleine Duvic, who has extensive experience and expertise in the area of cutaneous lymphomas. Here are highlights from her presentation:

- Two French dermatologists are responsible for the discovery of mycosis fungoides (Dr. Jean-Louis-Marc Alibert) and Sézary Syndrome (Dr. Albert Sézary) in the 1800’s;
- Sézary Syndrome is a triad of symptoms, typically

Scientific Conference Highlight...continued on page 14

4. da Silva Almeida AC, Abate F, Khiabani H, Martinez-Escala E, Guitart J, Tensen CP, Vermeer MH, Rabadan R, Ferrando A, Palomero T. The mutational landscape of cutaneous T cell lymphoma and Sézary syndrome. *Nat Genet.* 2015 Dec;47(12):1465-70
5. Kiel MJ, Sahasrabudhe AA, Rolland DC, Velusamy T, Chung F, Schaller M, Bailey NG, Betz BL, Miranda RN, Porcu P, Byrd JC, Medeiros LJ, Kunkel SL, Bahler DW, Lim MS, Elenitoba-Johnson KS. Genomic analyses reveal recurrent mutations in epigenetic modifiers and the JAK-STAT pathway in Sézary syndrome. *Nat Commun.* 2015 Sep 29;6:8470
6. McGirt LY, Jia P, Baerenwald DA, Duszynski RJ, Dahlman KB, Zic JA, Zwerner JP, Hucks D, Dave U, Zhao Z, Eischen CM. Whole-genome sequencing reveals oncogenic mutations in mycosis fungoides. *Blood.* 2015 Jul 23;126(4):508-19
7. Woollard WJ, Pullabhatla V, Lorenc A, Patel VM, Butler RM, Bayega A, Begum N, Bakr F, Dedhia K, Fisher J, Aguilar-Duran S, Flanagan C, Ghasemi AA, Hoffmann RM, Castillo-Mosquera N, Nuttall EA, Paul A, Roberts CA, Solomonidis EG, Tarrant R, Yoxall A, Beyers CZ, Ferreira S, Tosi I, Simpson MA, de Rinaldis E, Mitchell TJ, Whittaker SJ. Candidate driver genes involved in genome maintenance and DNA repair in Sézary syndrome. *Blood.* 2016 Jun 30;127(26):3387-97
8. Mishra A, La Perle K, Kwiatkowski S, Sullivan LA, Sams GH, Johns J, Curphey DP, Wen J, McConnell K, Qi J, Wong H, Russo G, Zhang J, Marcucci G, Bradner JE, Porcu P, Caligiuri MA. Mechanism, Consequences, and Therapeutic Targeting of Abnormal IL15 Signaling in Cutaneous T-cell Lymphoma. *Cancer Discov.* 2016 Sep;6(9):986-1005
9. L.K. Ferrarelli. HDAC inhibitors in solid tumors and blood cancers. *Sci. Signal.* 20 Sep 2016: Vol. 9, Issue 446, pp. ec216
10. Halsall JA, Turner BM. Histone deacetylase inhibitors for cancer therapy: An evolutionarily ancient resistance response may explain their limited success. *Bioessays.* 2016 Nov;38(11):1102-1110
11. Chen Y, Yang F, Zubovic L, Pavelitz T, Yang W, Godin K, Walker M, Zheng S, Macchi P, Varani G. Targeted inhibition of oncogenic miR-21 maturation with designed RNA-binding proteins. *Nat Chem Biol.* 2016 Sep;12(9):717-23

Finding a Miracle the Hard Way: Barbara and Victor Bartolome



Victor and Barbara Bartolome

My happy, fun, optimistic, and very tall ex-NBA pro basketball player husband, Victor, was diagnosed with mycosis fungoides (MF), a sub-type of cutaneous T-cell lymphoma (CTCL), in 1995. His condition had been misdiagnosed by his general practitioner, which is common, and

his small area of skin plaque had been previously treated

as psoriasis. We pursued a second opinion when the “psoriasis” began rapidly spreading. The dermatologist we sought out ordered punch biopsies and correctly diagnosed the MF, referring us to an outstanding oncologist at our local cancer center. As we learned more about the MF, we decided to also engage a cutaneous lymphoma specialist at a university medical center to oversee our case, and to work closely with our local oncologist for Victor’s ongoing care.

Victor embarked upon various treatment plans that covered about 15 years of continuous care, experiencing alternating periods where the MF either remained stable or progressed. He progressed from light box (PUVA) to oral medication (bexaroten), from topical ointments (nitrogen mustard,) to three successive types of treatment (romadepsin, liposomal doxorubicin (“doxil”), brentuximab vedotin). Through all of these stages, we saw varying degrees of control over the MF plaque and tumors that ultimately covered 40% of his 7’0” tall body.

The romadepsin infusions were only administered nine times before it had to be stopped, due to side effects that Victor could not tolerate. Victor successfully received the doxil infusions over four years, with no adverse side effects. Unfortunately, he reached the maximum lifetime dosage level of the doxil and the cutaneous lymphoma specialist advised he could not receive additional infusions of it. It was then suggested he begin a new type of treatment, named brentuximab vedotin (BV).

Victor began the infusions of BV, spaced three weeks apart. He experienced neuropathy in his feet and fingers after 3-4 infusions. By the 6th BV infusion, most foods had lost their taste and his appetite had greatly diminished. Around the 8th infusion, he began experiencing strong and consistent bouts of nausea and was eating less than one-fourth of his normal food intake. He regularly needed to take anti-nausea pills to get any food to stay down, as well as to combat intermittent dry heaves. As a result, by the 12th BV infusion he had lost a total of about 20 lbs., which took him down to 187 lbs. - substantially underweight for his tall body. He was weak and listless.

At our next visit, we told the doctor that we wished to stop the BV treatments immediately, stating that Victor simply couldn’t continue to tolerate the life threatening level of BV side effects that he was experiencing. The

doctor agreed and we were asked to return in six weeks. When we returned to the specialist six weeks later, Victor’s worsening skin plaque and tumors were examined but no specific treatment options were suggested. I felt frustrated and inquired as to what our options were for treatment. The doctor mentioned that Victor could possibly participate in an upcoming clinical trial that would take place there, but it would require us to spend an extended time period in that distant city. We asked if another university’s medical center might have options we should consider, and were informed that the options were very

limited. We left that visit feeling concerned and scared.

Upon our return home, I immediately sprang into action and began asking my physician contacts for suggestions on how to move forward with Victor’s case. A local internal medicine physician friend referred me to a personal friend of his, whose brother had struggled with lymphoma. In our conversation, she spoke very highly of her brother’s treatment of lymphoma, then kidney cancer, and then brain cancer, via Stanford Health Care (SHC) at Stanford University Medical Center. I called and scheduled an

“Victor embarked upon various treatment plans that covered about 15 years of continuous care...”

“I felt frustrated and inquired as to what our options were for treatment.”

appointment for Victor in September 2016. A private pilot friend informed me that a non-profit group called Angel Flight West would be happy to arrange a private pilot and their plane to fly us to Stanford for the medical appointment, free of charge. I was astonished. They arranged for two wonderful Angel Flights, up and back for Victor's visit, saving us a very long drive.

The day of our visit arrived. We checked in and were escorted to an exam room. We were shocked and amazed as eight individuals walked in and joined us to examine Victor and review his previous medical treatments with us: a cutaneous lymphoma oncologist, a radiation oncologist, a hematologist/oncologist, a dermatologist, a research specialist, and several nurses. This medical team's warm, considerate, open and friendly manner quickly put us both at ease. They left the room to confer over the case. Soon, they returned to discuss the group's top three suggestions for handling Victor's MF with us; advising us of the side-effects we could expect from each suggestion. The #1 suggestion was to begin a three week course of total skin electron beam therapy (TSEBT), which is low-dose, skin deep radiation. They fully and carefully answered all our questions and we agreed to schedule Victor's TSEBT treatments in October 2016.

Victor's three weeks of TSEBT treatments gave us a lot of time at the hospital to meet many others on the medical team and administrative staff; we simply could not be more impressed with the high level of consideration and customer service that we saw in every interaction! We discovered that, at the time Victor received his treatments there, Stanford was the only West Coast facility with the TSEBT machine. Listening to our concerns over Victor's weight loss, the physicians started Victor on Actimmune (Interferon gamma-1b) to boost his immune system and suggested he take a multivitamin. They scheduled us to see a nutritionist to discuss Victor's dietary needs. We were so pleased that the team considered all aspects toward Victor's good health!

Over the following three weeks of treatments, Victor noticed visible, ongoing improvements in his skin plaque and tumors. We returned home, and over the next 5-6 weeks, his skin was miraculously 100% resolved of every visible sign of the mycosis fungoides! In the past 25 years, he hadn't ever been clear of the awful MF skin plaque and

tumors. We couldn't believe the miracle that we had hoped and prayed for, for so long, had actually occurred!

“Over the following three weeks of treatments, Victor noticed visible, ongoing improvements in his skin plaque and tumors.”

We returned in late-January to show our excited medical team the fantastic TSEBT results and they were all so happy and excited for us! After hugging us and examining him, they advised that Victor's MF would likely stay under control for a 1-3 year period. He may then need another TSEBT treatment, sometime in the future. Victor was literally doing a daily happy dance... and it's so fun to see him enjoying this big miracle!

Victor's case will be added to the hospital database, hopefully helping other physicians and MF patients around the world. We feel that Victor's story might assist MF patients to see that it's

important not to give up hope and to be diligent in seeking out a medical team that will work closely with you... and really care about your outcome. Not every facility has the same treatment options, search out second opinions along the way and see what might be a new treatment option. If it's a long distance to other resources, check into Angel Flights at www.angelflight.com.

We felt that the hospital team really exceeded our expectations with their expertise, kindness, and excellent patient care, so we took the time to submit a compliment form on each team member. We also wrote a compliment letter outlining our great experience and sent it to the hospital CEO! We're now part of the wonderful hospital family, and we simply couldn't be more thankful! ✨

“...it's important not to give up hope and to be diligent in seeking out a medical team that will work closely with you...”

Editor's Note: The Cutaneous Lymphoma Foundation encourages each person to advocate for personal wellness by finding a medical team that meets personal expectations for care. We do not endorse one facility over another.

Scientific Conference Highlights ...continued

- 80% of patients present with red skin, larger lymph nodes and unusual cells in the blood;
- In Dr. Duvic's experience, patients don't always fit into the pre-defined boxes of the disease;
- 10% of all CTCL patients are the leukemic variant - which would include both MF & SS;
- Must have more than 1,000 circulating cells, have type-2 helper phenotype and through flow cytometry, have CD4+, CD26-, CD4+C7- V beta antibodies;
- T-cell receptor V beta-2 common in SS;
- Major initiative in 1996 to creating the HUT102 and HUT78 cell lines by Drs. Francine Foss and Paul Bunn to facilitate in-depth research;
- Understanding how these cancerous T-cells form in general has helped to move the study of this disease further;
- Sézary Syndrome is now thought to be a distinct disease from MF because of central memory T-cells and the specific markers of CD4+C26- or CD7-;
- Learning more now about rare subtypes like cutaneous gamma delta T-cell lymphomas along with primary cutaneous CD4+ small/medium sized pleomorphic T-cell variants;
- Interesting finding that SS cells have lost a lot of tumor suppressors. Specific pathways (P-53 and c-Myc) along with the intra-cellular environment can be targeted with new therapy;
- We do not know what specific molecules (antigens) are responsible for inducing the immune response that stimulates MF or SS cells to become cancerous;
- Some of the drugs used commonly can cause MF to occur and can be a reaction pattern with hydrochlorothiazide (most prescribed blood pressure medicine in the world). If you can get it early and stop the drug, MF will go away.
- Serotonin update inhibitors (antidepressants), Gleevac and anti-convulsants can be a cause of MF as a drug-induced disease which goes away once the drugs are stopped.
- Exposure to chemicals can be implicated;
- Infections like chlamydia and DNA viruses may also be a cause;
- Still looking for epidemiology studies as to the causes. Epidemiology studies are difficult and large grants are required to conduct them;
- First randomized trial for CTCL was in 1989. The study compared the combination of electron beam radiation and chemotherapy with topical therapy in the initial treatment of MF (Drs. Francine Foss and Paul Bunn);
- The second trial which wasn't randomized but a larger CTCL study, showed extracorporeal photopheresis (ECP) had a higher response rate in erythrodermic patients conducted by Dr. Alain Rook;
- 60-70% of SS patients have staph infections;
- Moisturizers are incredibly important and work better than steroids for flaking skin;
- Found that if there is a deletion in the programmed cell death pathway (PD-1/PD-L1), overall survival is significantly less;
- More research needs to be done to answer the question - why do some people have large cell transformation? Difference in African Americans than white populations died faster with large cell transformation;
- Increasingly more sophisticated in the ways we measure the biomarkers;
- More research needs to be done on gene function and apply all the knowledge to curing MF/SS;
- Interleukin-31 (IL-31) is a protein that plays a role in managing inflammation and is important for itch and in developing anti-itch medications;
- Rational combination therapies may prevent early resistance;

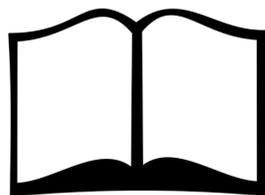
Dr. Duvic concluded that there are still many questions that need to be answered. However, the continued hope for these meetings is to make inroads into the questions that still remain, share the knowledge and develop new ways of diagnosing, treating and managing patients in the best way possible.

United States Cutaneous Lymphoma Consortium Annual Workshop March 2, 2017, Orlando, FL

Each year the United States Cutaneous Lymphoma Consortium (USCLC) hosts a cutaneous lymphoma specific workshop the day before commencement of the American Academy of Dermatology annual medical conference. The participation in this meeting has been increasing each year, with 100 participants joining this year's meeting. In general, the participants are from the United States, with a few international experts. One of the exciting trends in all the meetings has been the number of younger researchers, scientists and clinicians in attendance. The knowledge that is being shared and the passion of these young clinicians to learn from the seasoned experts inspires hope for patients that this important work will continue into the future.

Latest research findings:

- One of the most important molecules relating to cancer is called p53. Mutations of this molecule are seen in 40% of advanced stage MF but not in early stage MF;
- The FAS gene provides instructions for making a protein that is involved in cell signaling. Mutations in the FAS gene are seen approximately 10% of MF patients;
- A few studies have looked at MF & SS genomic information but nothing has come out of the studies to confirm specifically what is driving the disease;
- Historical gene sequencing was Sanger sequencing and shotgun sequencing. The last 5 years have seen an impressive boom in technology for rapid high quality next generation sequencing. A genome can now be sequenced in 26 hours and can offer personal sequence for \$999;
- Next generation sequencing has been developed for cutaneous lymphoma in the last few years. Over six papers researched over 100 genomes in cutaneous lymphoma, each looking at different aspects. Some SS, some MF or mix of both diseases.
- “UV signature” is a term used to define the type of ultraviolet light induced modifications of cells. UV signatures was found in many studies of cutaneous lymphoma patients with 75% of Sézary patients showing C-T transitions, which are consistent with UVB exposure. These modifications were seen in patients with and without light therapy. The conclusion being this type of cell modification comes from the accumulation of UV light over time in most people and not specifically from UV light treatments;
- The initial genomic analysis showed no single driver mutation found for cutaneous lymphoma. The analysis showed numerous genes and pathways are impacted, the behavior of a variety of cells and cell instructions play a role, cell signaling cell death cycles are involved with a lot of crossover among them all;
- Targetable understanding of these mutations in the biology of the cells and new therapies, using data for prognostic markers are critical to understanding patient outcomes and aid in treatment decisions;
- The biological mechanisms that lead to the disease state of cutaneous lymphoma is not a singular process. Treatments need to be identified and utilized to treat specific targets in patients. Development of a cutaneous lymphoma genomic panel is important. ☞

Making a Difference***Thank you for helping us make a difference!***

Your support allows us to provide quality information through our Online Learning Center and produce over 26,000 pieces of literature that are distributed to patients around the world



Your support made possible 14 Live Educational Events



Your support facilitated connections with people in 130 countries last year

Your generosity makes a big difference in our ability to impact the lives of people affected by cutaneous lymphoma. Your support is critical.

Please consider making a donation today by using the enclosed envelop or online at www.clfoundation.org/giving-online.

Every dollar counts! ☞

THERAKOS/Mallinckrodt Pharmaceuticals Opportunity



Are you or a loved one living with cutaneous T-cell lymphoma (CTCL), and receiving treatment with THERAKOS® photopheresis therapy? CTCL patients and

their caregivers may have an opportunity to help empower the CTCL patient community by sharing their experiences of CTCL and treatment with photopheresis therapy with others. If selected, patients and caregivers may participate in a program sponsored by Mallinckrodt Pharmaceuticals to provide their insight through print materials, on a website, at live events, and/or through video. These opportunities may include sharing their experiences with photopheresis therapy for CTCL.

Patients or caregivers who are interested may find out more by calling toll-free at (844) 514- 6288 or emailing llynch@snow-companies.com. Please see full Important Safety Information and Prescribing Information online at <http://www.therakos.com/important-safety-information-hp> ☞



CUTANEOUS LYMPHOMA FOUNDATION

PO Box 374
Birmingham, MI 48012

TIME SENSITIVE MATERIALS ENCLOSED



Learn

Will you be there?

Annual 2-Day Patient Conference

Greater Los Angeles Area

Saturday, June 24 through Sunday, June 25, 2017



Connect

Conference highlights include:

- Clinical Presentations
- Patient and Caregiver Roundtables
- Open Q&A Discussions with Medical Professionals
- Health & Wellness Presentations
- Updates on Research and Clinical Trials



Celebrate

Register TODAY to enter our drawing for

2 FREE nights at the Manhattan Beach Marriott

Visit our website for details: www.clfoundation.org/2DayLA