



# WHAT IS IMMUNOSUPPRESSION AND WHEN DOES IT HAPPEN?

With the onset of the coronavirus pandemic, many individuals voiced concerns about the relationship between cutaneous lymphoma and immunosuppression. There is no simple answer to the question: Are people with cutaneous lymphoma immunosuppressed/compromised? The simplest answer to this complex question is, it depends. In addition to any unrelated cutaneous lymphoma factors, a person’s specific diagnosis, stage and treatments are all part of determining whether someone is immunosuppressed/compromised or not.

What does it mean to be immunosuppressed? The National Cancer Institute defines immunosuppressed as “Having a weakened immune system. People who are immunosuppressed have a reduced ability to fight infections and other diseases. This may be caused by certain diseases or conditions, such as AIDS, cancer, diabetes, malnutrition, and certain genetic disorders. It may also be caused by certain medicines or treatments, such as anticancer drugs, radiation therapy, and stem cell or organ transplant. Also called immunocompromised.”

In October, 2021, we asked Dr. Alejandro Gru to address the topic of immunosuppression and cutaneous lymphoma in an online webinar. The following is a summary of the information that Dr. Gru shared.



## Background Information

T-cells and B-cells, which are lymphocytes, play a critical role in the body’s defense against external organisms. They also have a role in the generation of autoimmune conditions where, for example, there is an exaggerated immunologic reaction from our system that drives it into diseases that are related to the excessive responses from lymphocytes.

Taken from the “WHO Classification of Tumours and Haematopoietic and Lymphoid Tissues”, the charts on page 10 are a list of cutaneous T- and B-cell lymphoma variants. The WHO Classification provides clinicians with a methodical and comprehensive way to categorize cutaneous lymphomas. T cells are the more common resident cells in the skin, which explains why there are more patients with cutaneous T-cell lymphoma than cutaneous B-cell lymphoma.

Doctors use multiple ways to determine what kind of cutaneous lymphoma a patient has. They

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## 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. ❧

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## FORUM

The newsletter of the Cutaneous Lymphoma Foundation  
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#### 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.

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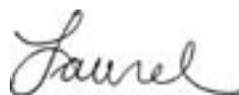
Spring is here and so are the budding flowers and trees, longer days and warmer weather - signs of new life.

A few weeks ago, the Foundation's Board of Directors gathered for one of our three annual meetings. With discussions around strategy and vision, and how the Foundation continues to work toward ensuring all people with cutaneous lymphomas have access to the best care possible, we recognize there is still so much to be done. So, with the vision of a life free of cutaneous lymphoma, and the mission of providing education, promoting awareness, advancing patient care and fostering research, with you, we will continue to work toward achieving these goals.

With that, you might have noticed throughout late winter and spring, the Foundation's programs focus on delivering information about cutaneous lymphoma research. This is largely due to your feedback and the overwhelming response indicating research and treatments are some of the biggest areas of interest. Therefore, in the following pages we are excited to share more information about immunosuppression, current clinical trial updates, and highlights/outcomes from the European Organization for Research and Treatment of Cancer (EORTC) meeting. Equally as important, we share with you one patient's story highlighting how he was deeply impacted by his experiences in a clinical trial.

We, the Foundation's Board and staff, hope you recognize how important you and your needs are in guiding the future of the Foundation. As we continue to plan and develop programs and services for the cutaneous lymphoma community, you and your voice matters in what comes next.

Please be well, stay safe and keep in touch. Happy spring to you and yours.




**"We hope you recognize how important you and your needs are in guiding the future of the Foundation"**

**Laurel Carlson**

## FROM THE CHIEF EXECUTIVE OFFICER

Susan Thornton



**"...To have a research poster from a patient organization accepted into a scientific meeting... shows the clinical/research community's interest in quality of life from the patient perspective."**

**Susan Thornton**

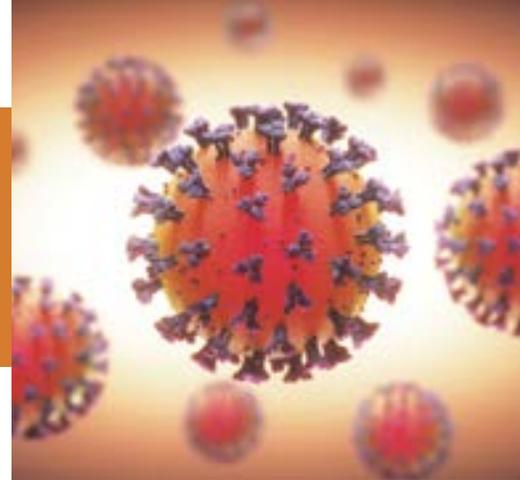
This is our annual issue dedicated to research. The term research has many meanings and takes many forms. It can be about new treatments currently in a clinical trial; it can be preclinical research seeking to find answers to essential questions that help understand how cutaneous lymphoma works in our bodies. An exciting new area of research is around capturing the "real-world experience" of individuals living with all forms of cutaneous lymphomas. It might also be studies conducted after completing a clinical trial to gather a deeper understanding of how a new therapy is working in a broader patient population.

In this issue, we bring you highlights from the scientific meeting held in Marseille, France, which was themed "Translating Science into Patient Care." Throughout the two-day conference, 55 individual presentations were delivered. An additional 68 poster presentations were available for viewing. The topics covered a wide range, from biologic insights

and preclinical studies to treatments, histopathology, epidemiology, and quality of life. I'm proud to share that the Cutaneous Lymphoma Foundation, along with our partner, the Lymphoma Coalition, had a poster accepted based upon the responses to

*From the CEO...continued on page 9*

# Frequently Asked Questions COVID-19



We asked Dr. Jasmine Zain, cutaneous lymphoma specialist and member of the Cutaneous Lymphoma Foundation’s Medical Advisory Council, to respond to COVID-related questions of interest to the cutaneous lymphoma community:

## **With a new study that vitamin D deficiency contributes to the risk factors for COVID-19, should I increase my vitamin D supplements?**

This is one study but it is suggestive that adequate vitamin D levels may be associated with improved outcomes after a COVID-19 infection. However, outcomes from serious infection are influenced by many factors including vaccination status, underlying health conditions, etc. If your vitamin D levels are low, then it is a good idea to supplement with vitamin D with the advice of your doctor.

## **Does sunscreen block vitamin D from the sun?**

Sunscreen prevents sunburn by blocking UVB light. Theoretically, that means sunscreen use lowers vitamin D levels.

## **What is the difference between an epidemic, a pandemic and an endemic?**

An epidemic means an outbreak of infection or sudden increase in cases of an infection in a certain area. A pandemic is an infection that is present worldwide. An endemic means that the infection or condition is regularly found among particular people or in a certain area.

## **If I just had COVID, am I protected against getting a severe course of COVID in the future?**

The data on this is not clear. You can still get an infection especially as new variants emerge.

## **Is there any information about a fourth shot for those who are immunocompromised?**

The CDC recommends a booster dose for moderate to severely immunocompromised patients. This is only for Moderna and Pfizer at least five months after the 3rd dose. In these patients, the course of 3 vaccines is the primary dose and the 4th is considered a booster.

## **Is the COVID-19 vaccine just as safe for people with cancer as they are for cancer-free individuals?**

An article was recently published in JNCCN (Journal of the National Comprehensive Cancer Network), and they have reported on the largest published peer-reviewed study examining short-term adverse effects of mRNA COVID-19 vaccination in patients with cancer - finding they experienced no more, and no different, side effects. These vaccines are safe for use in cancer patients. However, it is recommended that before any vaccination, patients should consult with their treating doctors. Certain conditions like bone marrow transplant and certain chemotherapies may interfere with your ability to mount an immune response. 

*Please note: Dr Zain responded to these questions in March, 2022. Please be sure to check the CDC website for the most current and up-to-date recommendations.*



Don't miss out, make sure to subscribe to the Cutaneous Lymphoma Foundation's YouTube channel (CutaneousLymphomaFnd) and follow us on Facebook and LinkedIn.

# EORTC-CLG SCIENTIFIC MEETING: CUTANEOUS LYMPHOMA - TRANSLATING SCIENCE INTO PATIENT CARE

The annual EORTC-CLG (Cutaneous Lymphoma Group) scientific meeting was held in Marseille, France, on October 14-16, 2021. The meeting is one of three scientific gatherings specifically dedicated to cutaneous lymphomas. Clinical updates and insights are shared and important research findings relevant to diagnosing, treating and understanding this group of rare diseases are presented.

The 2021 meeting was well attended, allowing both in-person and virtual participation by clinicians, researchers, scientists, industry and the Cutaneous Lymphoma Foundation. General topics covered were biologic insights, preclinical studies, treatment impacts, histopathology, epidemiology and quality of life from around the world.

Common themes of many of the presentations included:

- Challenges diagnosing cutaneous lymphoma variants
- The impact of delayed diagnosis on disease progression and effectiveness of treatment
- Leveraging new technologies, such as artificial intelligence, to create better options for early diagnosis
- Experience with newly approved and available treatments and recommended methods for their use

One of the valuable outcomes of the scientific meeting is the exchange of real world experience between the clinicians. For example, clinicians sharing their experience with new treatments is critical to learning how these therapies work beyond the narrow parameters of a clinical trial or how they may work in combination with other therapies.

While it is always exciting to learn about new treatments, exchanging experiences related to

tried and true therapies is also critical; especially how new technologies can provide greater insights on how existing treatments work within the context of the disease or interact with other treatments. Given the diverse nature of each individual's disease presentation and underlying biology, it's important to gather these insights so that treatments and treatment protocols can be modified and documented as new understanding comes to light.

In addition to the clinical and scientific presentations, outcomes from quality of life studies were also presented. Quality of life is an important consideration for anyone managing any form of cancer or rare disease. For individuals living with cutaneous lymphoma, the external visibility of the disease, the associated itch and pain, and the related emotional impact can all negatively affect quality of life. Also discussed were the challenges associated with diagnosing and providing early treatment accessibility for people of color.

Quality of life is still understudied; larger, more indepth research is required to determine new and better approaches for helping people manage these issues, while ensuring that all people are diagnosed properly, in a timely manner, and have access to the care they need. It's exciting to see the interest from the clinical and research community in the quality of life data. Better understanding of the issues faced by a wide range of individuals living with cutaneous lymphoma can be translated into improved care and support of all aspects of an individual's life beyond diagnosing and treating the disease itself.

Read additional details and highlights from the EORTC-CLG scientific meeting at [www.clfoundation.org/eortc-clg2021](http://www.clfoundation.org/eortc-clg2021)



# MY JOURNEY WITH CUTANEOUS LYMPHOMA

Shared by Paul J. - The Netherlands

Four decades cannot be summed up in a nutshell, so this is a long story.

## The Onset

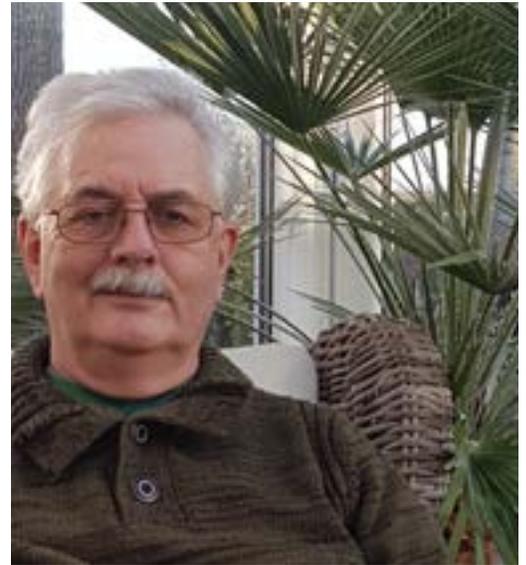
In the early 80's I had some strange red spots, especially on my hips and buttocks, but because it hardly bothered me, I didn't immediately go to a doctor. During a doctor's appointment, they saw it, and that's how I ended up on a merry-go-round for years to find out what it was. One thought allergy, another suspected eczema, the next psoriasis. Whatever they prescribed for it, nothing helped. In 1992, I came to Prof. Willemze in Amsterdam. After ruling out a few things, I had a number of biopsies taken. I was then diagnosed with stage I mycosis fungoides. Because just over 10% of my skin was affected, it became 1B.

I started UVB treatment. Treatment started as a few seconds the first time, each time a little more. After three months, I was at about six minutes. After the first weeks, it seemed to get a lot worse, light pink spots turned bright red and spots appeared that I hadn't noticed before. I was shocked, but later it turned out that is the case with almost everyone. Gradually the spots faded, and after about three months I was almost completely 'clean.' The treatment was stopped and check-ups were eventually reduced to once every six months. After a while, another spot appeared and for that I was given corticosteroid ointment (Dermovate). Three years after being diagnosed, I was prescribed another UVB treatment.

In the decades that followed, this cycle repeated itself over and over and I actually had very little trouble with it. Around the turn of the century, I moved to Dubai for a year and a half and during that period I really didn't have one small spot. Could this be because of the difference in the amount of sun? Over the years, the period between successive UVB series did appear to increase. I hardly had to use Dermovate anymore. The skin almost never changed, and the lymph nodes were still not swollen.

Shortly after I moved in 2012, a slightly larger spot appeared on my right hip. The dermatologist (who was well acquainted with CTCL because he had once done an internship in Leiden) suggested irradiating it locally with electrons. It became painful, the skin cracked, and it was very unpleasant. Thick scabs appeared, and after a few weeks, during which I had to do my utmost not to scratch them because of the intense itching, the scabs fell off spontaneously.

As early as 1992, I requested more information about our rare condition. At the time I had understood that it was a skin condition that in a small number of cases could degenerate into cancer, so I wasn't too concerned. A



Paul J.

patient folder (literature) was in the making. Every now and then I asked again about it, but the folder was not ready yet.

## Finding Others

With the advent of the Internet, bulletin boards and mailing lists, I was given other opportunities to search for information. I ended up at an international Yahoo group where fellow sufferers from all over the world could exchange experiences. Finally, someone who experienced the same (or usually slightly different) experience! The group moved to a dedicated server and still exists: <http://listserv.acor.org/archives/CTCL-MF.html>

There were very few other Dutch people in that group, and those who were there did not live nearby. I did read that there were regular meetings of fellow sufferers, especially in America, but also in London. I was able to attend such a meeting at St Thomas' Hospital in London. A nurse gave a presentation on how to keep your skin in good condition and how to combat itching as much as possible. It was interesting, but even more fun, to come face-to-face with a number of fellow sufferers for the first time! We decided to see if we could organize something similar in the Netherlands, and around 2010, a small group of fellow sufferers met twice in a small room in a catering facility. Unfortunately, they didn't get a sequel after that.

With the rise of Facebook, a closed group arose from the listserv. Here, mainly practical experiences were exchanged

and emotions were shared. A German-speaking group also emerged from the English-speaking group and when it turned out that there would be interest in it, I decided to start a Dutch-speaking group of fellow sufferers on Facebook. We now have more than 100 participants and can share experiences with each other without language problems and without others being able to watch.

We had our first meeting day in 2018. About 300 fellow sufferers, partners and caretakers attended. Various specialists gave a presentation, and I was allowed to tell something about what it means to be a patient with such a rare condition for decades. I couldn't help but emphasize that I would be very curious about the patient folder, which had been promised since 1992. We were given the solemn promise that it would really come one day.

The day was a success and turned out to meet a great need. Mutual contact with fellow sufferers was helpful, but there is an increasing need from the specialists for organized contact with their target group. It was decided to set up an organization of volunteers to shape this. This was worked out in a number of meetings in Utrecht, where we were allowed to use the facilities of IKNL Netherlands. After weighing up the pros and cons, we preferred a foundation to an association. We searched

**It was interesting, but even more fun, to come face-to-face with a number of fellow sufferers for the first time!**

and found enthusiasts for a board, a patient council (of which I am a part) and a medical advisory council. The Skin Lymphoma Foundation Netherlands was born.

The second patient day took place at the Leiden University Medical Center on 12 October 2019. Here the foundation was presented to the public for the first time. We're just getting started and still figuring

out how to best serve the interests of everyone with cutaneous lymphoma. For this, we sought (and found) cooperation with various organizations, including the Platform for Rare Cancers.

### Doing My Part

After being in almost full remission for over 10 years, I recently had a couple patches appear. This may have been a blessing in disguise as these patches made me eligible for



a clinical trial. I am participating in research at The Center for Human Drug Research CHDR Foundation in Leiden for Mycosis Fungoides (MF). Twenty MF patients and 10 healthy test subjects are taking part in the study.

Research CHDR1947 has two objectives: primarily to investigate disease-related characteristics and so-called biomarkers (characteristic abnormalities in cells, for example) for MF, and secondly, to investigate differences over time and/or between different patients of those biomarkers before and after treatment with chlormethine (CL) gel (Ledaga, known elsewhere as Valchlor) and examining skin reactions after using CL gel.

A diagnosis of MF is very difficult to make. The only method so far is taking a skin biopsy and having it assessed by a specialist. Because the condition is very similar to much more common conditions such as psoriasis, it often takes years before the correct diagnosis is made. This research hopes to find other ways that may enable a much earlier diagnosis.

Finding enough volunteers with MF is just as difficult. In The Netherlands, the diagnosis is only made in about 75 people per year, and not everyone meets the desired criteria. Due to privacy legislation, it is not possible to simply distribute a targeted call for participation, for example via the treatment centers. As a result, not all potential participants are reached. Of course, not everyone wants to participate in a study. I myself had never taken part in such a scientific study

*My Journey...continued on page 8*

## My Journey...continued from pg 7

before, but given the importance for my fellow sufferers and because of my innate interest in science, I registered anyway.

As a participant, I will visit Leiden a total of seven times. The first time was a comprehensive survey to make sure I met all of



the entry criteria. I received a detailed explanation about the research and the consequences that participation has as a test subject. This is followed by a total of six research days.

The first is a kind of baseline measurement. Heart film, blood and urine tests, taking skin samples with special plasters and cotton buds, extensive photos; regular, in 3D and with infrared

cameras; measurements with special equipment on the skin for redness, thickness of the 'spots,' moisture permeability of the skin, and so on, were taken. I also received a smartwatch and smartphone to take home. With this, I will keep a kind of diary about how much itching, pain and insomnia I experience. The smartwatch registers how much I scratch in my sleep at night.

The second examination day follows after a few weeks. Even more measurements were taken, two skin biopsies of spots with and without MF and using a vacuum pump, two blisters are generated from which the fluid is extracted. It was not so bad for me because I expected that I would experience more trouble from it. It took about 5 hours but how time flew by! The research team really made every effort to put me at ease as a test subject. All questions (the more the better, I get the

impression) are answered in detail and there is plenty of time for a friendly chat. After this second day, I was allowed to start applying the Ledaga on the spots. Only three times a week for the first few weeks.

The CL gel is a 'cytostatic,' an agent that prevents cell division (of the 'bad' T cells) and thus tackles the cause of the spots. It must be handled with all kinds of precautions. It had to be applied very thinly. Because I can't see all my spots well, my wife helps me with the application. After the first weeks, there was almost no difference visible and after weighing the tube it turned out that we had done that 'thin spreading' a bit too literally. After the third research day, application was to be done slightly less thin and increased to daily.

On the fourth research day, this turned out to have obvious results. A few spots had already faded quite a bit, but most were heavily discolored. Brown-red was a sign that the activity of the T cells had decreased, bright red that the (healthy) skin also reacted strongly to the drug. Although it itches and stings a bit more than before, the total nuisance is still not too bad for me.

April 13th will be my fifth research day and my last day will be May 10th. The study will then continue with participants who started later, and the 10 healthy subjects. The latter do not receive Ledaga, but their biomarkers must of course not show false positive reactions.

Although the study will probably not have been completed by then and it will be too early to be able to present clear conclusions, the intention is to give a presentation on the next patient day that the Dutch Cutaneous Lymphoma Foundation will organize next autumn. Hopefully, I will be able to tell you something about how you can experience this as a 'guinea pig.' I can already say very positively! 🐷

**To find clinical trials currently  
recruiting participants, visit**

**[www.clfoundation.org/directory](http://www.clfoundation.org/directory)**

## 2-DAY PATIENT CONFERENCE UPDATE

We recently requested your participation in our 2-Day Patient Conference survey where we asked you, the members of our community, about your interest/comfort with gathering in person for this year's event. It has been a challenging couple of years for all of us, and while we were all hoping to be able to return to an in-person event this year, based on your responses and guidance from our Medical Advisory Council, we have made the decision that this year's 2-Day Patient Conference will again be held virtually, July 8-9, 2022, with no in-person option.

This year's conference will feature two tracks, one for those who are newly diagnosed and another for those further along in their journey.

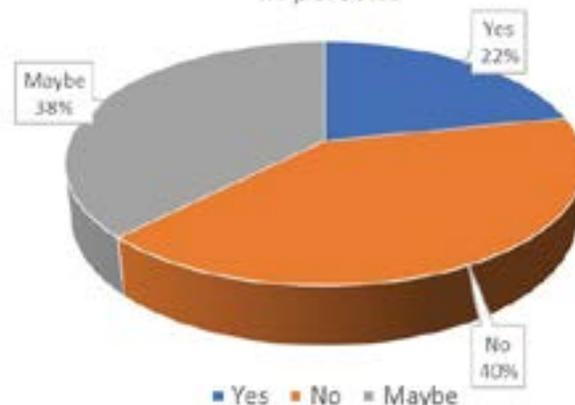


Registration for the 2-Day is available at <https://bit.ly/3KaVycy> or use the QR code on the left.

We want to thank everyone who participated in the survey and also share some additional details on the survey results. COVID concerns were a major factor in the community's decision on not wanting to attend an in-person conference. We also saw that attendees are more comfortable with the virtual format.

We hope to see you all, virtually, in July!

Would you attend the 2-Day Patient Conference in person?



### From the CEO...continued from pg 3

the 2020 Global Patient Survey entitled "A cross-sectional study examining the diagnosis and psychosocial experience of patients with cutaneous lymphoma." It's a big deal to have a research poster from a patient organization accepted into a scientific meeting. It shows the clinical/research community's interest in quality of life from the patient perspective. A high-level overview is provided in the pages that follow, and a more detailed version can be found on the website. As you can imagine, taking that much scientific data and condensing it into a few paragraphs is a challenge. Still, we have done our best to share what we thought would be the most interesting to the patient community.

You will also find a discussion about immune suppression in cutaneous lymphoma from Dr. Alejandro Gru and answers to your most pressing questions by Dr. Jasmine Zain. Highlights from this year's Rare Disease Day advocacy event with congressional representatives and our featured patient story round out the issue.

I wish there was a way to share everything that has happened in the world of cutaneous lymphoma with you on these pages, but the Forum would be too long to read. Know that

we continue to stay connected to the research world every day to make sure you have access to the latest knowledge.

As always, if you have questions, want to know more about what's happening in the research arena, reach out or engage directly with your peers on the Community Connections platform. You help make this work come to life with your questions and insights about your experience living every day with cutaneous lymphoma.

I love to share what Dr. John Zic said at one of our educational forums:

*"Every day somewhere in the world, the light is on in a lab, and someone is working on cutaneous lymphoma research."*

There is always hope and light to lead us forward.

Be well, my friends,

Immunosuppression...continued from pg 1

will review skin lesions, pathological findings, what they see under the microscope, and what markers these abnormal cells have in the skin. This information can then be translated into clinical and pathological findings that allow physicians to determine a specific diagnosis.

**The Immune System and Infections**

While the cause of cutaneous lymphomas is not known, it is important to remember that with the disease there is a dysregulation of the immune system. T cell lymphocytes have certain responses that are critical in immunologic reactions against infections, tumors, etc. It is believed that with cutaneous lymphoma there is an impaired mechanism of host T cells to actually create an appropriate immunologic response to defend the body from bacteria, viruses, etc. When the disease progresses, for example, if it goes from patches or plaques to tumors or develops in the blood, there is a significant increased susceptibility to infection.

Infections need to be paid attention to because they can lead to more significant issues, especially for individuals with Sézary syndrome where the disease circulates in the blood.

Signs of progression may include:

- advanced skin involvement - BSA (body surface area), tumors/erythroderma
- involvement of sites other than the skin
- large cell transformation (change to larger cells, rapid growing)
- increased LDH (blood marker of disease, more than skin)

It is important to remember that most individuals with early stage disease will not progress during the course of their disease, but rather, will stay in the limited patch/plaque or generalized plaque stage of the disease.

**Treatments and the Immune System**

One outcome of the pandemic was the publication of United States Cutaneous Lymphoma Consortium (USCLC) treatment guidelines in the American Academy of Dermatology’s Journal. The guidelines provide clinicians with an understanding of what medications, in general, are considered safe and nondisruptive to the immune system and which ones should be restricted to those patients who require a more aggressive treatment. The guidelines divided the different diseases and their corresponding treatments into four major categories: low-risk, intermediate-low-risk, intermediate-high-risk, and high-risk.

**Low-Risk**

Low-risk treatments are associated with early stage

**Cutaneous T- and B-cell Lymphoma Variants**

Cutaneous T-cell Lymphomas (75%-80% of cutaneous lymphomas)	Mycosis fungoides
	Sézary syndrome
	Primary cutaneous CD30+ lymphoproliferative disorders
	Folliculotropic mycosis fungoides
	Lymphomatoid papulosis
	Primary cutaneous anaplastic large cell lymphoma
	Primary cutaneous extranodal natural killer/T-cell lymphoma, nasal type
	Primary cutaneous peripheral T-cell lymphoma
	Primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma
	Primary cutaneous aggressive CD8+ T-cell lymphoma
	Subcutaneous panniculitis-like T-cell lymphoma
Cutaneous gamma-delta (γδ) T-cell lymphoma	

Cutaneous B-cell Lymphomas	Primary cutaneous follicle center lymphoma (PCFCL)
	Primary cutaneous marginal zone B-cell lymphoma (PCMZL)
	Primary cutaneous diffuse large B-cell lymphoma, leg type (PCLBCL-LT)
	Primary cutaneous diffuse large B-cell lymphoma, non-leg type

disease such as mycosis fungoides (MF), pagetoid reticulosis, lymphomatoid papulosis, and primary cutaneous (PC) marginal zone or PC follicle center B-cell lymphoma. These are conditions that could be handled very safely with skin-directed therapeutic approaches.

There are multiple low-risk therapies such as topical retinoids, mechlorethamine gel or ointment, topical steroids with or without occlusion, imiquimod, home narrowband ultraviolet (UV)B phototherapy, heliotherapy, oral antibiotics, oral anti-pruritics, diluted vinegar or bleach soaks/baths and aggressive moisturization. These therapies are safe, not suppressive of the immune system, and do not make the patient predisposed to infection.

**Intermediate-Low-Risk**

The next stage of variants of more advanced disease, but still considered low risk, are primary cutaneous anaplastic

large cell lymphoma, folliculotropic MF, granulomatous MF, MF stages IB (extensive patches/plaques) and subcutaneous panniculitis-like T-cell lymphoma.

Some intermediate-low-risk treatments are oral retinoids (bexarotene, acitretin, isotretinoin), methotrexate, oral steroids, vorinostat and interferons (alpha or gamma). These can create some side effects that could include reducing your total number of white blood cells and could put you at a slightly higher risk of developing infections, but in general are safe.

### Intermediate-High-Risk

Intermediate-high-risk patients are patients with MF stages IIB (tumors) and III (erythrodermic), primary cutaneous diffuse large B-cell lymphoma (non-leg type). For intermediate-high-risk and high-risk patients, treatments may at times expose patients to some degree of immunosuppression.

### High-Risk

High-risk would be Sézary syndrome, MF stage IV or transformed, primary cutaneous gamma-delta T-cell lymphoma, CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma, extranodal natural killer/T-cell lymphoma, primary cutaneous diffuse large B-cell lymphoma leg type.

For those that have significant progression in their disease, treatment may have consequences, especially those that require aggressive treatment.

High-risk therapies that more likely than not could create issues with the immune system and could predispose patients to a higher risk of infection, include pralatrexate, romidepsin, mogamulizumab, brentuximab, gemcitabine and other chemotherapies and skin radiotherapy, photopheresis and office-based UV therapy (because of travel during pandemic).

## The Impact of Biologics and Targeted Therapies

As more is learned about the disease, it is clear that the use of biologics and targeted therapies have created a major change in the way patients with cutaneous lymphomas are being treated. Studies show significant patient responses to these therapies indicating better treatment. Additionally, it is encouraging that new monoclonal antibodies and immune modulators used to treat other cancer conditions are also useful to modulate the immune system and may lead to much better and less toxic responses.

**Alejandro Gru, MD**

Dermatopathology Division and Fellowship Director  
University of Virginia

Dr. Gru's full presentation is available on the Foundation's YouTube channel: <https://youtu.be/1gZF41wpaiY> 

# Frequently Asked Questions

## Can UVB light treatment cause skin cancer?

Different types of ultraviolet light are used to treat cutaneous T-cell lymphoma. Narrow band UVB is used the most. It is very precise in its availability to both kill off cutaneous lymphoma cells in the skin and reduce the symptoms and the signs you see. It gets rid of itch and redness by reducing inflammation in the skin. While no treatment is without inherent risk, for the most part, narrow band UVB is not a potent causer of skin cancer; however, with hundreds of treatments, it may increase your chance of skin cancer, especially if you are someone who is at risk for developing skin cancers.

## Is the prognosis the same for interstitial mycosis fungoides as regular mycosis fungoides?

Interstitial mycosis fungoides is an uncommon subtype of mycosis fungoides. The prognosis is similar to other subtypes, depending on how extensive your lesions are and how thick they are. The biggest prognostic factor would be if you have just patches and plaques and thin lesions, or if you are developing tumors.

**Keri Chaney, MD**

Assistant Professor - Dermatology  
Froedtert - Medical College of Wisconsin

Questions and responses taken from the recording of our "Answers From the Experts: Quarterly Q&A - January 2022" webinar. For the full-length recording, please visit: <https://youtu.be/dDqomTFOoQ0>

# DRUG DEVELOPMENT: AN OVERVIEW OF THE CLINICAL TRIAL PROCESS FOR MECHLORETHAMINE AND MOGAMULIZUMAB

We recently sat down with Dr. Steven Horwitz and Dr. Ellen Kim to discuss the following drugs that have gone through the clinical trial process. We wanted to learn what work led to the trial, what had to happen for the trial to occur, what was learned during and after the trial, and what is next.

## Mechlorethamine (Valchlor)

**What was the origin of mechlorethamine as a possible treatment for cutaneous lymphoma?** Valchlor gel has a long history going back to the 1940s when it was first approved by the FDA as a systemic agent for a variety of lymphomas to be given by IV. In the 1950s, mechlorethamine started being used topically for mycosis fungoides. It was compounded as an aqueous solution that you would dilute with water and paint on, or as a compounded ointment that you would get from a compounding pharmacy. However, its topical use wasn't officially FDA approved.



**“Like many efforts in our community, (the PROVe study) took a village.”**

**Ellen Kim, MD**

In the mid 2000s, Dr. Stuart Lessin led a multicenter effort to perform a randomized, controlled, non-inferiority study to look at a version of mechlorethamine gel, also known as Valchlor. The study compared the gel to the compounded ointment and showed that it was just as good as the compounded ointment, with about a 40% to 50% overall response rate by mSWAT scores.

With Valchlor being on the market since 2013, there was interest in what we call its “real world” use; for example, how are our patients using it? How are our doctors prescribing it? Were they prescribing it with other types of therapies? We wanted to get more information about how it was really used in daily practice. So that led to PROVe, which stands for “Prospective Observational,” a US-based study assessing the outcomes, adverse events, treatment patterns, and quality

of life in patients with mycosis fungoides, cutaneous T-cell lymphoma.

**What had to happen for the PROVe study to occur?** Like many efforts in our community, it took a village. This was a multicenter trial. It was first sponsored by Actelion, who was the company that had the rights to Valchlor. Actelion was instrumental in constructing the protocol, as well as organizing all of the CTCL experts to get involved. They recruited 41 sites, both academic and community-based, throughout the US. Once constructed, the protocol had to get approved by the FDA and then approved at all the different trial sites. And, of course, we had to ask our patients to enroll. We needed to recruit 300 patients, and for our small community, that does take a little while.

The study took a big group effort, but it was real world. The plan was to enroll patients who were already actively using Valchlor and coming into the clinic. They would be asked whether they'd be interested in enrolling in this trial. We took the information normally collected during a clinic visit and submitted it to the clinical trial data collectors. We submitted questionnaires to the patients and compiled their data. We asked all kinds of questions: How often were you using Valchlor? What was your stage of disease? What other treatments were you on? What were your side effects? What were the effects on your quality of life?

**What was learned during the PROVe study of Valchlor gel?** This study was one of the biggest studies conducted in a prospective observational way. It took two years and we enrolled 301 adult patients across 41 sites. One interesting thing we found was that not only were early stage patients using Valchlor gel, but also patients with advanced disease who were using it in addition to whatever systemic therapies they were on. We also learned that patients were applying it mostly once a day, which is the recommended application that was studied in the original 2013 trial by Dr. Lessin. It was also being utilized every other day, every three days, with different dosing regimens, all likely reflecting the doctors giving recommendations to manage side effects.

**What are the side effects?** Similar to the previous trial, this phase four observational trial showed that this medicine is very safe. It's not absorbed systemically, but the main effects are local skin side effects, which include irritation, contact dermatitis (like an allergic contact dermatitis), and itching.

Side effects were less frequent than were seen in the 2013 study where about 20% of patients had to stop the study due to the skin side effects.

In the PROVe study, we basically saw that the incidence of these skin adverse events, or side effects, was less. It could be because these patients in the real world were not just on Valchlor. They were also on topical steroids, phototherapy, or internal agents such as bexarotene and other types of systemic agents. We did see the use of a lot of combination therapies. It is possible that if a patient is on topical steroids as well as Valchlor, that the irritant and allergic dermatophytic side effects could be less. That is one hypothesis.

The most gratifying thing that was learned is that the longer patients used Valchlor, the better they got. We learned that Valchlor gel can take 18 months of treatment before full responses are seen. Remember, this is a real world study which is different from a clinical trial where you get approval for an agent. Patience is key, and you need to continue to follow a treatment for the long haul. The quality of life questionnaires given to patients showed that those who responded to Valchlor gel, also showed improvement in their health-related quality of life based on the Skindex-29 questionnaire. So we could see that not only were there clinical responses to Valchlor, but those who did respond, also saw improvement in their quality of life. This real world study provided a lot of great information.

#### ***What's next with the Valchlor gel or mechlorethamine gel?***

From these studies, we now know several factors:

- we have had an FDA approved agent since 2013,
- we know that Valchlor gel can take a while to work but can be safely combined with other therapies, and
- it also improves quality of life.

We now have more objective data for what we've known for a long time; Valchlor gel is an important skin-directed therapy for CTCL. It is definitely effective for early stage patients, but also helpful for palliation or adjunctive care for advanced stage patients. Additionally, now that Valchlor is FDA approved, insurance coverage is much easier than previously. Going forward, we'd like to try to further explore combination therapies with Valchlor gel. We'd like to also explore its long-term safety, and then try to understand whether any of the dosing regimens provide a recommended way to mitigate the skin side effects.

## **Mogamulizumab**

***What was the origin of mogamulizumab as a possible treatment for cutaneous lymphoma?*** Antibodies are proteins that can usually bind certain features on a cell surface. This ability allows them to engage in the immune system in the destruc-

tion of cancer cells. This capability has been used in oncology treatments for at least 25 years and has been researched even longer.



**“Investigators are continuing to study how to extend the benefits of this therapy”**

**Steven Horwitz, MD**

One of the most successful antibodies that we routinely use is rituximab. It is targeted to CD20 - a marker and antigen on the surface of most B-cells and, therefore, most B-cell lymphomas. Investigators in Japan applied a similar approach with T-cell lymphomas, identifying CCR4 as a marker antigen on the surface of certain T-cells, including a very difficult to treat lymphoma, adult T-cell leukemia lymphoma (ATLL). This often aggressive lymphoma is commonly found in the area of the world near Japan and the Caribbean. The researchers also looked for other lymphomas that expressed CCR4 - a therapeutic target for the same antibody as ATLL. They identified mycosis fungoides and Sézary syndrome, two of the more common subtypes of cutaneous T-cell lymphoma (CTCL).

***What had to happen for the trial to occur?*** What led to the early clinical trials of mogamulizumab for cutaneous lymphoma was this development of an antibody for a similar but different disease (ATLL), and the recognition that the same therapeutic target was present on the cells of many patients with CTCL - specifically mycosis fungoides and Sézary syndrome.

Initial early studies led by investigators, including those at Stanford and MD Anderson Cancer Center, identified mogamulizumab as a reasonable therapy for CTCL. It then took investigators from around the world and the sponsor, Kyowa Kirin, to bring everyone together to do a very large randomized study (MAVORIC) in a very rare disease. It was a worldwide effort of people coming together to try to study and explore this new treatment for cutaneous T-cell lymphoma - both to define how well it works and compare it to an existing standard therapy, in this case, Vorinostat, a FDA-approved oral medication approved in the United States for CTCL.

# RARE DISEASE WEEK ON CAPITOL HILL

Representing the cutaneous lymphoma community, the Cutaneous Lymphoma Foundation participated in Rare Disease Legislative Advocates (RDLA) 2022 Rare Disease Week on Capitol Hill in March. The legislative conference and Hill days were held virtually once again this year, allowing those who were not able to travel to Washington, DC, to participate in this important event. The conference is hosted by the EveryLife Foundation for Rare Diseases, a nonprofit patient advocacy organization focused on rare diseases.

The conference provided the opportunity to learn more about the issues that impact the rare disease community as a whole, as well as those that affect specific diseases. Hours of preparation prior to the actual legislative meetings ensures that the advocates have an opportunity to be well informed on the legislative “asks,” while crafting their personal stories of how these issues impact them or their loved ones personally.

The Foundation’s legislative focus was H.R. 6160, the Access to Rare Indications Act. In brief, the act would require Medicare and Medicaid to cover a drug used in the treatment or management of a disease or condition affecting 200,000 or fewer individuals - the definition of a rare disease - if such use is supported by clinical criteria.

The bill would also require health insurance plans to provide an expedited mechanism for formulary exceptions, reconsideration, and appeal of any coverage denial for off-label use of a drug for a rare disease patient that meets these criteria. This bill could make a significant difference in the quality of life for rare disease patients who experience barriers to care because the most effective treatment for their condition is off-label.

The ability to join our voice with hundreds of other rare disease advocates helps to strengthen our message. We are grateful to have the opportunity to participate in this annual legislative event. 🌸



**RARE DISEASE WEEK  
ADVOCACY**

**953 RARE DISEASE  
ADVOCATES**

**370 MEETINGS WITH  
CONGRESS**

**297 PATIENT ORGANIZATIONS**

**49 STATES + D.C., PUERTO  
RICO AND VIRGIN ISLANDS**

**1 AMAZING RARE DISEASE  
WEEK!**

## Drug Development...continued from pg 13

**What was learned?** Investigators learned a lot from the study’s top line data. It showed that individuals who received mogamulizumab were progression-free longer - meaning, their disease was controlled longer than those who received oral Vorinostat. In that sense, it was an advance in adding treatment tools for patients with CTCL.

Additionally, things were learned that may help individualize treatment. For instance, data showed that patients with blood involvement (Sézary syndrome), had the best results - some showed a complete response and others had responses that lasted a long time. Individuals with skin lesions and lymph node disease also responded, but those responses were less frequent.

The study data provided both an understanding of the overall activity, or benefits, of mogamulizumab, and how to better select or match patients to that therapy.

**What is next?** Investigators are continuing to study how to extend the benefits of this therapy, including combination stud-

ies. Combination studies look at combining mogamulizumab with other drugs that activate the immune system in different ways to see if a deeper response can be created - meaning more people getting completely, or nearly completely, better. Another study looks at using medications that also can stimulate the body’s immune system to make its own immune response against the cancer cells to see if the remissions can last a long time or be durable.

**Ellen Kim, MD**

Medical Director, Dermatology Clinic

Perelman Center for Advanced Medicine/Penn Medicine

To hear Dr. Kim’s full presentation on mechlorethamine, please visit <https://youtu.be/tTaodgaRmRc>

**Steven Horwitz, MD**

Medical Oncologist

Memorial Sloan Kettering

To hear Dr. Horwitz’s full presentation on mogamulizumab, please visit <https://youtu.be/DcQFQQoQALE> 🌸

# HELP ENSURE THE FUTURE OF THE CUTANEOUS LYMPHOMA FOUNDATION: CHARITABLE BEQUESTS

Including a charitable bequest to the Cutaneous Lymphoma Foundation in your estate planning is a wonderful way for you to benefit a cause that is important to you, and to leave a legacy. Charitable bequests are very flexible. With a bequest to the Cutaneous Lymphoma Foundation, you can make a commitment without spending anything now since the bequest will be paid upon your death and you wouldn't be dipping into your current assets or current cash flow. Your bequest can be easily changed down the road if you wish to modify it. And, depending on the size of your estate and the estate tax laws in effect as of the time of your death, your estate might benefit from estate tax savings.

A bequest included in your will or revocable trust is easy to set up with your attorney's assistance. Bequests usually are made in one of two ways...either a gift of a specific dollar amount (or a gift of a specific asset), or a percentage of your estate.

Naming the Cutaneous Lymphoma Foundation as a beneficiary of your retirement account or life insurance is a very easy way to benefit the Cutaneous Lymphoma Foundation. Your retirement account, or any portion of it, can easily be left to the Cutaneous Lymphoma Foundation. Upon your death, the funds held in your retirement account are distributed to the beneficiaries you have named in the "beneficiary designation" you have completed. You can name individuals or charities, or a combination of the two as beneficiaries, though care has to be taken when combining individuals and charities in one beneficiary designation. When retirement funds pass to an individual beneficiary, he or she must pay income tax on the amounts withdrawn (and there are often time restrictions specifying how quickly the funds must be withdrawn);

whereas, when the funds pass to the Cutaneous Lymphoma Foundation, the Cutaneous Lymphoma Foundation receives 100% of the funds...completely free of any income tax.

The Cutaneous Lymphoma Foundation can also be named as a beneficiary of a life insurance policy. It can also be named as a co-beneficiary with individuals, such as family members, or as a contingent beneficiary, to receive the funds if the primary beneficiary dies before the insured person.



Lastly, many states provide that beneficiary designations can be set up for bank or brokerage accounts. This is accomplished by setting up a "POD" (payable on death) or "TOD" (transfer on death) account at a bank or brokerage firm.

If you have any questions or would like to discuss this further, please contact the Cutaneous Lymphoma Foundation at 248-644-9014 or [info@clfoundation.org](mailto:info@clfoundation.org) and your personal estate planning attorney. ✍

## UPCOMING EVENTS & OPPORTUNITIES

### Join Community Connections

Make sure to check out the Cutaneous Lymphoma Community Connections, a place where you can interact with others facing the same or similar experiences as you. In order to provide privacy and encourage open communication with each other, Community Connections is open exclusively to patients and their loved ones.

To learn more, visit  
[www.clfoundation.org/connections](http://www.clfoundation.org/connections)

### Upcoming Events

To learn about upcoming events, visit  
[www.clfoundation.org/upcoming-events](http://www.clfoundation.org/upcoming-events)  
or scan the Q-code below.





**CUTANEOUS LYMPHOMA FOUNDATION**  
PO BOX 374  
BIRMINGHAM, MI 48012

**TIME SENSITIVE MATERIALS ENCLOSED**

## **Spring has arrived...and people are eager to get outside!**

### ***Are you preparing for an event?***

Maybe a 5k, 10k or a marathon, a Tough Mudder race, cycling event or any other type of competition. Want to make your training even more impactful by raising awareness and funds to support cutaneous lymphomas?

Well, here's your chance to turn your hard work into support for education, research and resources.

### ***Want to learn more?***

Call (248) 644-9014 ext 200 or email at [holly@clfoundation.org](mailto:holly@clfoundation.org)

### ***Ready to get started?***

Text **CLFriends** to **71777** or visit <https://app.mobilecause.com/vf/CLFriends> to set up your event today!

***Thank you to all our past, present and future fundraisers - we can't do it without you!***

