Cutaneous Lymphoma

Community Advisory Board Report

20 January 2022

LYMPHOMA
COALITION

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Introduction

Cutaneous T-cell lymphoma (CTCL) is a rare lymphoma that presents primarily in the skin but may also involve the viscera, lymphatic system, and blood.[i] The most common subtypes are mycosis fungoides and Sézary syndrome with visible skin alterations, pruritus, pain, and other conditions that may impact quality of life for patients. A chronic, relapsing course, the goal of treatment is to reduce the symptoms patients experience, preserve health-related quality of life, and prevent further disease progression.[ii]

The Lymphoma Coalition, in collaboration with the Cutaneous Lymphoma Foundation, hosted a cutaneous lymphoma Community Advisory Board Meeting on 20 January 2022 with Kyowa Kirin. Community Advisory Boards, also referred to as CABs, are groups of patient advocates and expert patients/carers. CAB members use their professional and/or personal knowledge and expertise to discuss and advise on the latest developments, challenges, and issues related to medical treatments and procedures under development in their respective disease area. CAB members are those who are living with the specific condition or alternatively, may be a close family member, carer, or member of a patient organisation that works within the disease to advance key priorities or address patient outcomes.

The virtual cutaneous lymphoma Community Advisory Board Meeting was hosted and moderated by Open Audience. Meeting participants included ten CAB members comprised of patients and patient advocates from nine countries, namely Austria, France, Italy, London, Portugal, Spain, The Netherlands, United Kingdom, and the United States (this person is based in the US but works globally, including leading a pan-European initiative coordinating patient advocacy group support for those affected by cutaneous lymphoma). Further, nine representatives from Kyowa Kirin joined the meeting, as well as three representatives from Lymphoma Coalition.

Prior to the virtual meeting, a pre-survey helped to inform and support robust meeting dialogue and engagement. Eight CAB members participated in the pre-meeting survey. As a result, we learned:

- 100% of participants indicated delays in diagnosis and/or misdiagnosis as a key issue.
- 100% identified itching as the medical concern that they felt impacted their quality of life the most, followed by 66% noting pain (66%) and fatigue (also 66%.)
- 100% shared that information on treatment for cutaneous lymphoma was the resource they were most interested in, followed by information about prognosis (87%) and symptoms (50%) respectively.
- 83% noted quality of life was a priority, followed by event-free survival without recurrence (66%) and overall survival after treatment (50%).
- 75% said that a lack of awareness by healthcare professionals contributed to delayed diagnosis.
- 72% indicated that their disease was initially misdiagnosed, with 57% receiving treatment for the misdiagnosed disease.
- 67% indicted that their physician did not articulate or share options surrounding clinical trials.
- 50% shared that it took more than two years to receive a formal diagnosis of cutaneous lymphoma.

- 33% reported that they had consultations with five doctors before receiving a formal diagnosis, and a further 17% saw four doctors before being diagnosed.

Participants were much more likely to positively rate information they found on their own about their disease than what was provided by their healthcare team at diagnosis. 57% found the information provided by their medical team was insufficient to make informed health decisions.

Participants really needed help understanding their disease and how to manage/cope with the daily impact on their life. One CAB member explained it like this:

"The main need is support for the day-to-day management of the disease. You get new lesions, sometimes similar, sometimes different and you don't know if it's the disease or something else. You have itching, you try not to scratch, but you do, you see how your skin is not well and how it is degrading, and that undermines you psychologically. If on top of that you do not see any progress in treating your disease, the future is too uncertain."

Another said, "It is really important to have a physician who provides context for the disease in order to allow the patient to come to terms their 'cancer' (a scary word), but which is for many (unfortunately not all) a chronic disease."

Two thirds of participants felt somewhat involved in decisions about their treatment. They would like to know more about the anticipated length of relief from using possible treatments and the success rate of each, while also understanding the potential side effects. Many felt they were not getting complete information.

The most important symptoms for treatments to control were skin infections and itchy skin, though respondents indicated this was difficult to prioritise as they knew some things can be more medically problematic (like infections) but other symptoms had a bigger impact on quality of life.

Participants indicated they would be willing to fill out surveys and questionnaires to get a better understanding of side effects of treatments, both intensity and persistence.

While patients prefer less invasive treatments and consider ease of treatment administration, priority is of course on how well the treatment works (including length of time before the next treatment is needed) and minimal side effects given the often-chronic nature of the disease.

The impact of cutaneous lymphoma on personal relationships is extensive, with 66% indicating it had impacted relationships with friends, a third having difficulties at work, and a further third having difficulties with their spouse or partner.

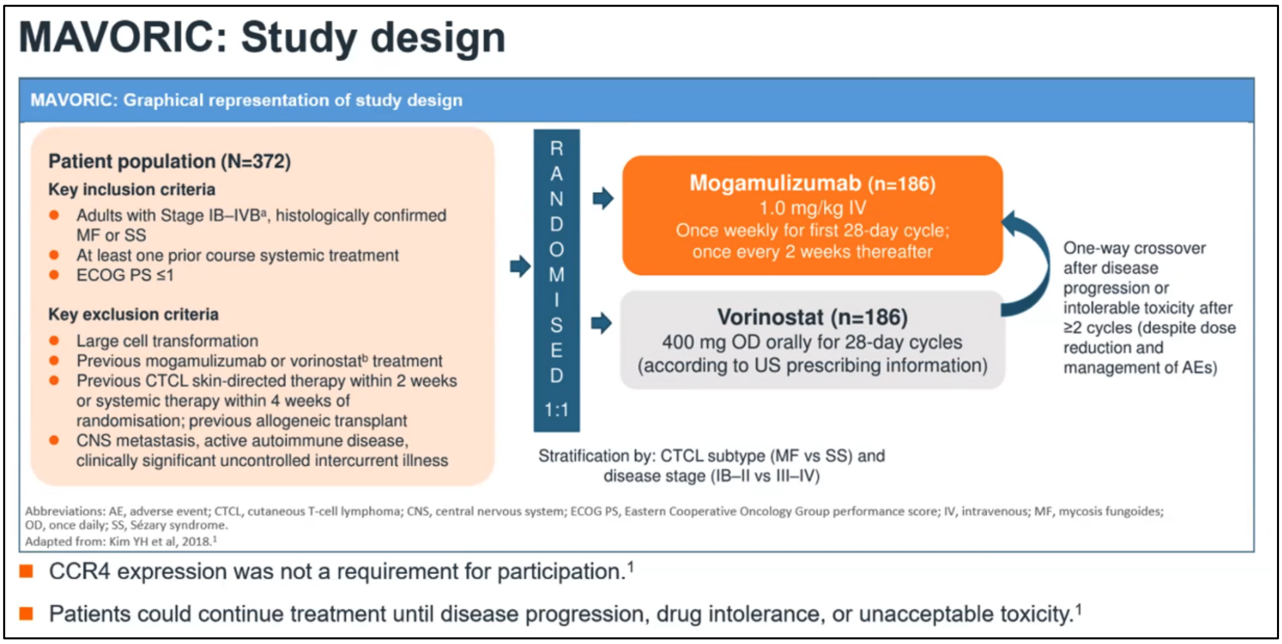
Mogamulizumab

Dr Jan-Paul Rosen, International Medical Affairs Director with Kyowa Kirin, provided a comprehensive overview of the history of mogamulizumab..

Kyowa Kirin has a longstanding history in the development of a novel approach to target T-cell lymphoma that spans more than twenty years. As early as 1996, Kyowa Kirin collaborated with external researchers to develop monoclonal antibodies against chemokine receptors, including CCR4. The work of Kyowa Kirin in the development of monoclonal antibodies gave rise to the drug mogamulizumab, with the clinical efficacy and safety of the drug demonstrated in the MAVORIC trial. [iii] Phase I studies began for patients with T-cell lymphomas in 2007, with the first regulatory approval in Japan in 2012, followed by commercial launches in the United States in 2018, and more recently Europe in 2020.

There are different international and country-specific guidelines that look at the latest evidence, primarily addressing where different treatment are (or should be) used, patient types or severity, with some of the guidelines currently being updated or having been recently updated. More specifically, these include the National Comprehensive Cancer Network (NCCN), European Organisation for Research and Treatment of Cancer (EORTC), European Society of Medical Oncology (ESMO), and the Dermatological Oncology Working Group (ADO).

Dr Rosen spoke to the MAVORIC study, noting details of the design as well as sharing some of the key endpoints and reported adverse events, as well as the importance of measuring blood involvement as it may impact survival.



MAVORIC: Study design

MAVORIC: Graphical representation of study design

Patient population (N=372)

Key inclusion criteria

- Adults with Stage IB–IVB[a], histologically confirmed MF or SS
- At least one prior course systemic treatment
- ECOG PS ≤1

Key exclusion criteria

- Large cell transformation
- Previous mogamulizumab or vorinostat[b] treatment
- Previous CTCL skin-directed therapy within 2 weeks or systemic therapy within 4 weeks of randomisation; previous allogeneic transplant
- CNS metastasis, active autoimmune disease, clinically significant uncontrolled intercurrent illness

RANDOMISED 1:1

Mogamulizumab (n=186)
1.0 mg/kg IV
Once weekly for first 28-day cycle; once every 2 weeks thereafter

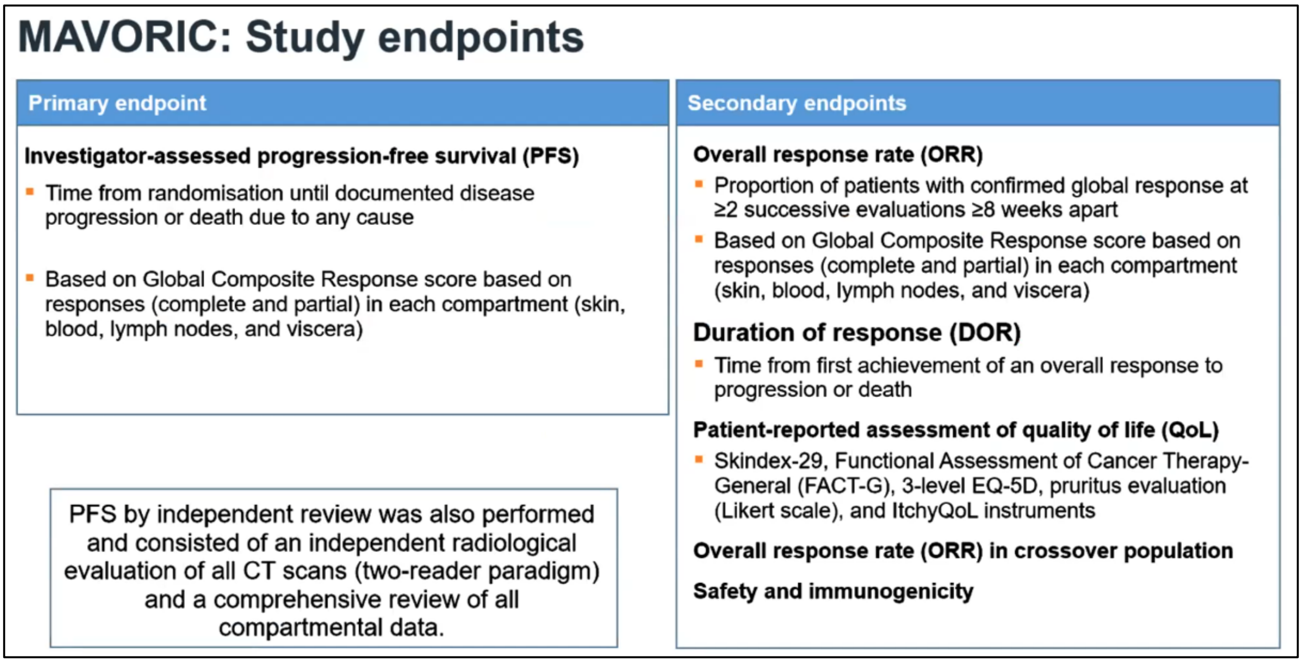
Vorinostat (n=186)
400 mg OD orally for 28-day cycles (according to US prescribing information)

One-way crossover after disease progression or intolerable toxicity after ≥2 cycles (despite dose reduction and management of AEs)

Stratification by: CTCL subtype (MF vs SS) and disease stage (IB–II vs III–IV)

Abbreviations: AE, adverse event; CTCL, cutaneous T-cell lymphoma; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance score; IV, intravenous; MF, mycosis fungoides; OD, once daily; SS, Sézary syndrome.
Adapted from: Kim YH et al, 2018.[1]

- CCR4 expression was not a requirement for participation.[1]
- Patients could continue treatment until disease progression, drug intolerance, or unacceptable toxicity.[1]



MAVORIC: Study endpoints

Primary endpoint

Investigator-assessed progression-free survival (PFS)

- Time from randomisation until documented disease progression or death due to any cause
- Based on Global Composite Response score based on responses (complete and partial) in each compartment (skin, blood, lymph nodes, and viscera)

PFS by independent review was also performed and consisted of an independent radiological evaluation of all CT scans (two-reader paradigm) and a comprehensive review of all compartmental data.

Secondary endpoints

Overall response rate (ORR)

- Proportion of patients with confirmed global response at ≥2 successive evaluations ≥8 weeks apart
- Based on Global Composite Response score based on responses (complete and partial) in each compartment (skin, blood, lymph nodes, and viscera)

Duration of response (DOR)

- Time from first achievement of an overall response to progression or death

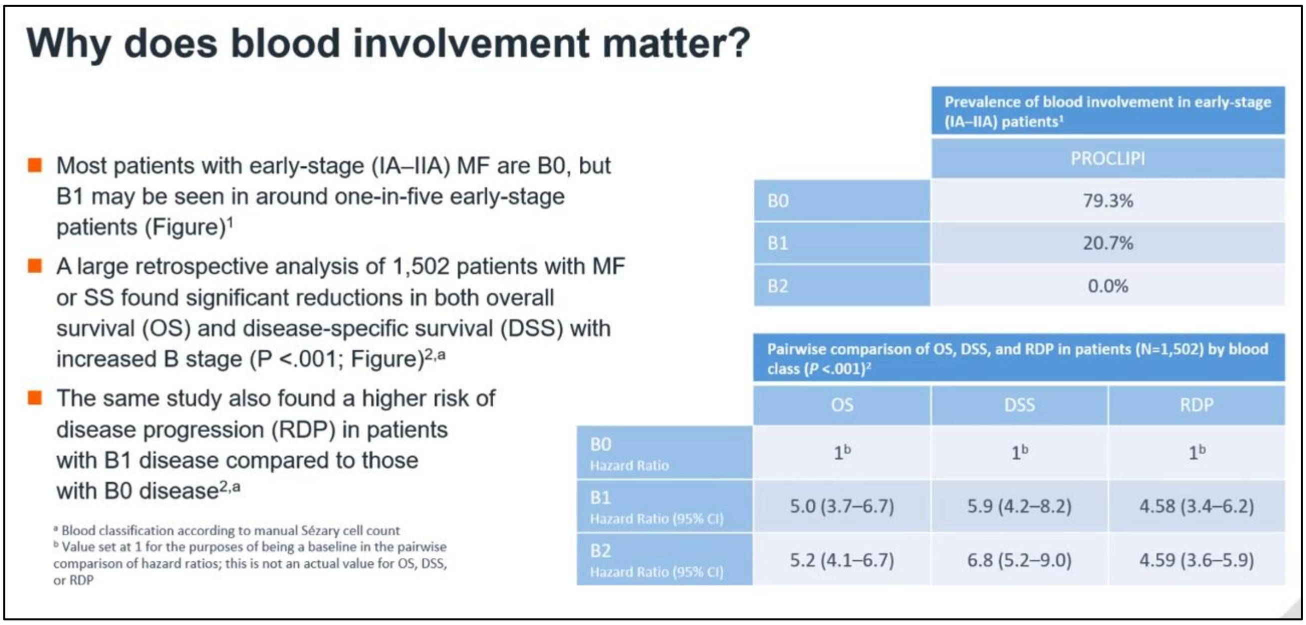
Patient-reported assessment of quality of life (QoL)

- Skindex-29, Functional Assessment of Cancer Therapy-General (FACT-G), 3-level EQ-5D, pruritus evaluation (Likert scale), and ItchyQoL instruments

Overall response rate (ORR) in crossover population

Safety and immunogenicity

PFS does include cross-over patients.



Why does blood involvement matter?

- Most patients with early-stage (IA–IIA) MF are B0, but B1 may be seen in around one-in-five early-stage patients (Figure)[1]
- A large retrospective analysis of 1,502 patients with MF or SS found significant reductions in both overall survival (OS) and disease-specific survival (DSS) with increased B stage (P <.001; Figure)[2,a]
- The same study also found a higher risk of disease progression (RDP) in patients with B1 disease compared to those with B0 disease[2,a]

Prevalence of blood involvement in early-stage (IA–IIA) patients[1]

	PROCLIPI
B0	79.3%
B1	20.7%
B2	0.0%

Pairwise comparison of OS, DSS, and RDP in patients (N=1,502) by blood class (P <.001)[2]

	OS	DSS	RDP
B0 Hazard Ratio	1[b]	1[b]	1[b]
B1 Hazard Ratio (95% CI)	5.0 (3.7–6.7)	5.9 (4.2–8.2)	4.58 (3.4–6.2)
B2 Hazard Ratio (95% CI)	5.2 (4.1–6.7)	6.8 (5.2–9.0)	4.59 (3.6–5.9)

[a] Blood classification according to manual Sézary cell count

[b] Value set at 1 for the purposes of being a baseline in the pairwise comparison of hazard ratios; this is not an actual value for OS, DSS, or RDP

From an observational perspective, there are known challenges experienced in clinical practice, notably:

- Challenges associated with the management of CTCL, with expectations currently driven by experience of existing therapies.
- Not all patients have their blood assessed by flow cytometry, an influential factor in some patients not receiving the treatment that is most effective for their disease.

- While there have been successful applications for reimbursement in first relapse or refractory MF or Sézary settings, mogamulizumab tends to be used by clinicians as a late intervention for those with severe disease.
- Patients are reporting early skin-related benefits, with wider benefits showing with subsequent treatment options.
- Some patients receive less than six months of treatment before discontinuation. For instance, the median time on mogamulizumab, as per the MAVORIC study, is 6 months, with a 20% drop off by the 4th cycle of treatment. (Please note, crossover patients are included in this data.)

The most common adverse events associated with the drug mogamulizumab are infusion reactions and "moga-rash." As noted by Kyowa Kirin, infusion reactions tend to account for very few patients discontinuing treatment, primarily as they can be pre-treated with an antihistamine or by altering the speed of infusion. Patients tolerate moga-rash with topical steroids, however, due in part to the unpredictability it is important to differentiate from disease progression so that patients do not stop taking the drug prematurely, which requires a biopsy of the affected skin.

WHAT WE HEARD FROM COMMUNITY ADVISORY BOARD MEMBERS	
💬	A recount of a patient experience, with initial fever and significant pain after the first mogamulizumab infusion. The second infusion brought palpitations for three days, but the pruritis slowly began to decrease.
💬	Other documented reports of reactions to the initial infusion include fever, chills, and intense symptoms in response or reaction to the swift death of the cancer cells (tumour lysis syndrome). It is important to document and share as a potential initial effect to allow patient management by their medical team, and to remain on the treatment.
💬	Even though the drug may have an amount of time it takes to infuse (an hour) and do follow up assessment, the amount of time the patient is in the clinic can be much longer depending on how busy the clinic is and how patients are processed.
💬	In Portugal, patients do not pay for treatment. However, in most cases patients are not involved in choosing their therapeutic option. In the country, mogamulizumab is not approved with only a handful of patients having early access to the drug.

WHAT WE HEARD FROM KYOWA KIRIN
To ensure patients information is relayed to clinicians, there are a variety of routes to share pertinent information that are supported by best practices, case studies and training. Where adverse events are present, recording information is a useful tool to help update relevant safety information in a timely and efficient manner.
Although hospitalization following the first infusion is not something frequently experienced, it can happen if the patient develops tumour lysis syndrome.
With respect to symptom control following cessation of mogamulizumab - specifically the length of time the effects persist - Kyowa Kirin does not collect information on how long symptom control lasted following cessation of treatment however, it is an area of interest. At present, this issue is being looked at in the trial programme, including a study that is currently underway that looks at treatment scheduling.
Understandably, there are challenges related to the amount of time required for some patients to travel every two weeks. While the infusion timeline (or actual process) takes an hour, there is an assessment afterwards that may extend the process by up to an additional hour.
In response to the implications of COVID-19, included lockdowns and challenges associated with patient access to healthcare facilities, Kyowa Kirin indicated that there are no active programmes currently in place for home infusion at this time. But it is possible for the infusion to occur at a clinic that is nearer to the residence of the patient, essentially removing the need for a patient to commute to a major teaching hospital.

Patient Experience with Cutaneous Lymphoma

Lindsay Perera, Patient Partnership Lead with Kyowa Kirin, introduced the patient journey in cutaneous lymphoma to explore insights, help overcome the challenges, and better understand the disease burden further.

In recent years, engagement activities and formal research conducted with patients and caregivers across Europe on the experience of living with the disease have helped to inform the Kyowa Kirin patient journey in CTCL, as well as support the development of a toolkit to help further increase insights and understanding of the disease.

There are key points when considering the patient journey. Namely:

- The patient journey - from itch to diagnosis to appropriate treatment - is not a linear pathway.
- Misdiagnosis is common.
- While topical treatments are of help in the short-term, symptoms return.
- The focus tends to remain on the initial single site of the disease on the body, rather than considering that it may be a systemic problem, leading to a loss of time before diagnosis.

There are four key elements prior to a formal diagnosis to take into consideration:

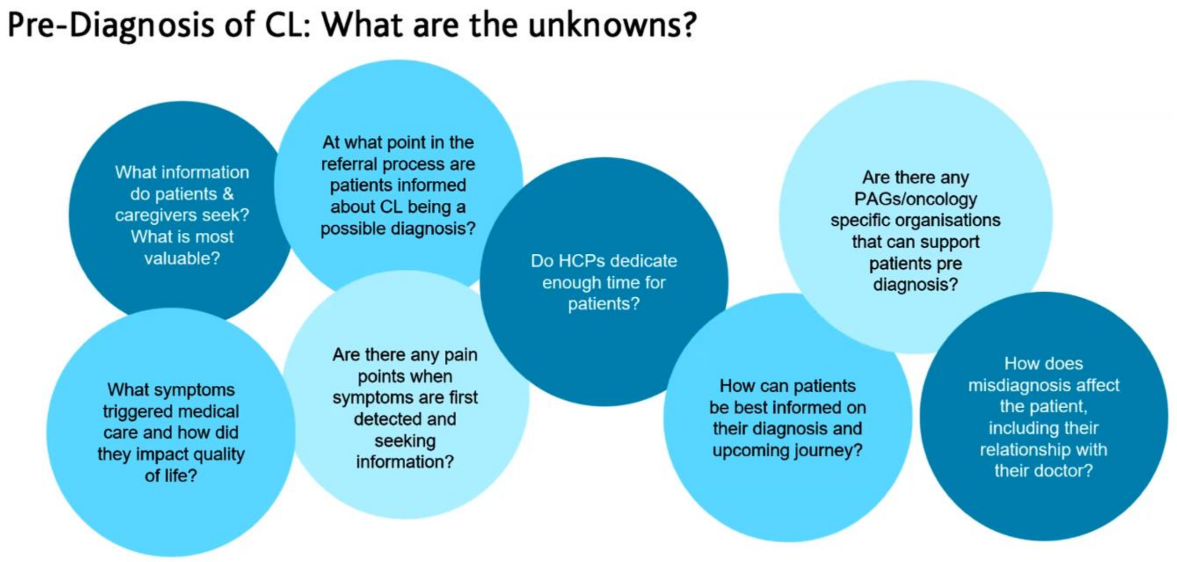
1. Far more often than not, the problem is presumed to be psoriasis or eczema. Healthcare professionals may need help to identify and act at this time, while patients may better recognize that their condition represents more than a skin disorder.

2. Healthcare professionals often dig deeper, just in the wrong place. This requires healthcare professionals to be more receptive to listening to what patients share rather than rely completely on established processes. Patients need to remain aware that there is potential for re-diagnosis or a new diagnosis at this stage.

3. There are life changing symptoms and challenging moments. Healthcare professionals need to be aware of alternatives and be open to considering other issues, like auto-immune diseases. Patients need to understand their rights, such as access to supports for themselves as employees, and for their carers.

4. It is hard to judge time when patients are repeatedly trying treatments. Healthcare professionals need a more defined timeframe for suspicion of cutaneous lymphoma, while patients require a means to accurately track “elapsed treatment time” to ensure they are equipped to have conversations about alternative diagnosis and treatment.[iv]

Pre-Diagnosis of Cutaneous Lymphoma



Pre-Diagnosis of CL: What are the unknowns?

What information do patients & caregivers seek? What is most valuable?

At what point in the referral process are patients informed about CL being a possible diagnosis?

What symptoms triggered medical care and how did they impact quality of life?

Are there any pain points when symptoms are first detected and seeking information?

Do HCPs dedicate enough time for patients?

Are there any PAGs/oncology specific organisations that can support patients pre diagnosis?

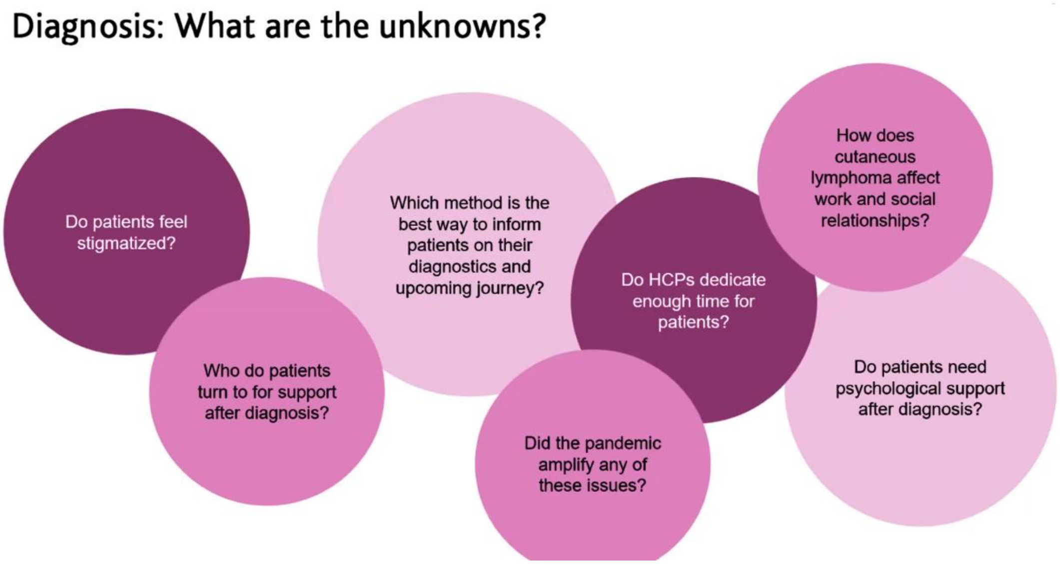
How can patients be best informed on their diagnosis and upcoming journey?

How does misdiagnosis affect the patient, including their relationship with their doctor?

With respect to the symptoms that triggered the need for medical care, as well as the lived experiences in relation to pre-diagnosis of cutaneous lymphoma, a lack of information is common and prevalent. As doctors are not widely aware of the disease, diagnosis is frequently late. Further, with a low level of knowledge by doctors, an experienced pathologist is often necessary to detect the problem, a challenge compounded by the lack of specialists.

WHAT WE HEARD FROM COMMUNITY ADVISORY BOARD MEMBERS	
💬	It was only when diagnosed with another type of lymphoma that a CAB member shared that their doctor investigated the skin problem. Observationally, there was a limited amount of information available, both for newly diagnosed patients and from the clinicians to the patient.
💬	Suffering from pruritis, a CAB member shared that their doctor initially thought it was an allergy. When the pruritis progressed to a rash, they went back to the doctor who suggested it might be eczema. While topical steroids helped the rash for a brief time, it did not help with the pruritis. After 10 months, they consulted with a dermatologist who, after numerous visits, took a biopsy which showed the disease.
💬	A lack of communication between patient and doctor was noted as a key factor that adversely impacted the relationship and eroded the level of trust one CAB member held with their general practitioner. This was instrumental in their decision to communicate instead with their specialist who explained things more thoroughly. Stressing the importance of doctors taking the time to speak to patients about what is happening and provide reassurance is key as too often this does not appear to be happening.
💬	The time in between suspicion and formal diagnosis (or the "limbo time") can have a significant impact. A CAB member shared that although their time to diagnosis was brief, efforts to shorten this part of the journey for all patients would be beneficial, highlighting that patient organisations or foundations might play a key role in helping patients during this phase.

Late Diagnosis



Diagnosis: What are the unknowns?

Do patients feel stigmatized?

Who do patients turn to for support after diagnosis?

Which method is the best way to inform patients on their diagnostics and upcoming journey?

Did the pandemic amplify any of these issues?

Do HCPs dedicate enough time for patients?

How does cutaneous lymphoma affect work and social relationships?

Do patients need psychological support after diagnosis?

Diagnosis of cutaneous lymphoma is frequently delayed or late. This extended process can have a considerable negative effect on patients. Late diagnosis may also be compounded by the fact these are rare diseases, and access to experts may be limited.

As most patients have early-stage disease when they start to seek help, the lymphoma is often difficult to detect even with the involvement of a dermatologist. At that point, a biopsy may not detect enough cancer cells to make a definitive diagnosis adding to the complexity and challenges, particularly in a community hospital setting. Additionally, if early blood tests results are normal, patients may experience challenges escalating their case to a specialist level. General practitioners are supportive in some cases, electing to refer patients for a biopsy and referring patients to a dermatologist.

WHAT WE HEARD FROM KYOWA KIRIN

Kyowa Kirin acknowledged a late diagnosis of cutaneous lymphoma, combined with a lack of communication or referrals to other doctors, may further undermine patient understanding of their diagnosis.

WHAT WE HEARD FROM COMMUNITY ADVISORY BOARD MEMBERS

In France, data gathered by a patient organisation survey revealed that late diagnosis is common, often involving numerous visits. This extended process has a considerable negative effect on patients. Additionally, according to the same survey data, many doctors do not inform their patient that it is a form of cancer during communication, contributing to psychological repercussions when the patient discovers this is the case.

In the case of a CAB member, their dermatologist was only able to advise that it was a cancer with no further information offered. After researching the issue on the internet, with the belief the cancer would be fatal, they located a doctor who understood the condition and took the time to sufficiently explain what was happening. Upon returning to the initial doctor, the doctor did not know any details about the disease or the appropriate treatment.

Diagnosis for another CAB member was relatively smooth as the dermatologist seemed to be aware of the condition and therefore, knowledgeable about how to treat and next steps. Only later, through dialogue with other patients, did they realise how lucky they were to get a quick diagnosis.

Formal Diagnosis

Accessing more information on treatment, prognosis and side effects is desirable. Dermatologists, haematologists, and general practitioners are viewed as the most likely sources of information however, knowledge and awareness are thought to vary considerably between healthcare professionals. At all stages, including formal diagnosis, transparent and effective communication between patient and doctor is paramount, however, communication challenges persist.

For instance, at a major international cutaneous lymphoma clinical meeting held in 2020, it was noted that the audience had been asked whether they used the word ‘cancer’ when diagnosing patients with mycosis fungoides or Sézary syndrome. At least half of the audience indicated they did not. While the intention to not create fear is important, it was viewed as naïve to assume that patients would not seek information themselves, discover they had cancer, and inevitably find worst-case scenarios.

With respect to feeling stigmatised by the diagnosis of cutaneous lymphoma, CAB members spoke to several issues they experienced ranging from psychological impacts to fears related to the disclosure of a rare cancer diagnosis in the workplace for fear of the impact on employment. Most did not have access to a psychologist as part of their care team.

<table>
<tr><th colspan="2">WHAT WE HEARD FROM COMMUNITY ADVISORY BOARD MEMBERS</th></tr>
<tr><td>💬</td><td>Given the responsibility of doctors to communicate honestly about disease and help manage expectations when patients undertake their own internet research, it would be beneficial for the medical team from Kyowa Kirin to ensure all side effects are being reported, captured, and communicated.</td></tr>
<tr><td>💬</td><td>Sharing information of a cancer diagnosis with others can be challenging. One member shared how they felt responsible for the reaction of others, making it even more difficult to discuss or share their diagnosis. Further, they spoke of how fortunate they felt to have a clinical psychologist as part of their care team. Conversely, another CAB member believed access to a psychologist would have been beneficial in helping manage how they communicated with their family and friends, particularly when struggling to communicate details of their diagnosis and disease management.</td></tr>
<tr><td>💬</td><td>Well-meaning inquiries from friends or family may also be challenging to deal with. One CAB member experienced such difficulties when needing to respond to inquiries, namely the number of times people asked how they were feeling, and the ensuing psychological effects those continuing questions presented.</td></tr>
<tr><td>💬</td><td>Living alone in another country at the time of diagnosis, a CAB member conveyed how they elected to share their diagnosis with select friends, but not with their employer. Rather, they tried to maintain a low profile about their condition. They had difficulties navigating the initial shock while concurrently entering the initial treatment sequence. Their advice to others was to pursue a treatment course that is effective but also considers lifestyle factors. The example they provided pertained to an initial treatment and the need to wear special glasses that made them feel very self-conscious, particularly in a work-related environment.</td></tr>
<tr><td>💬</td><td>With respect to the difficulty following a specialist diagnosis, the impact on the quality-of-life can be particularly challenging. A CAB member spoke of the need to constantly balance treatment with how they experienced a lack of clarity on practically living with the symptoms.</td></tr>
<tr><td>💬</td><td>Patients need help processing their disease, including the fact it is incurable, and managing expectations.</td></tr>
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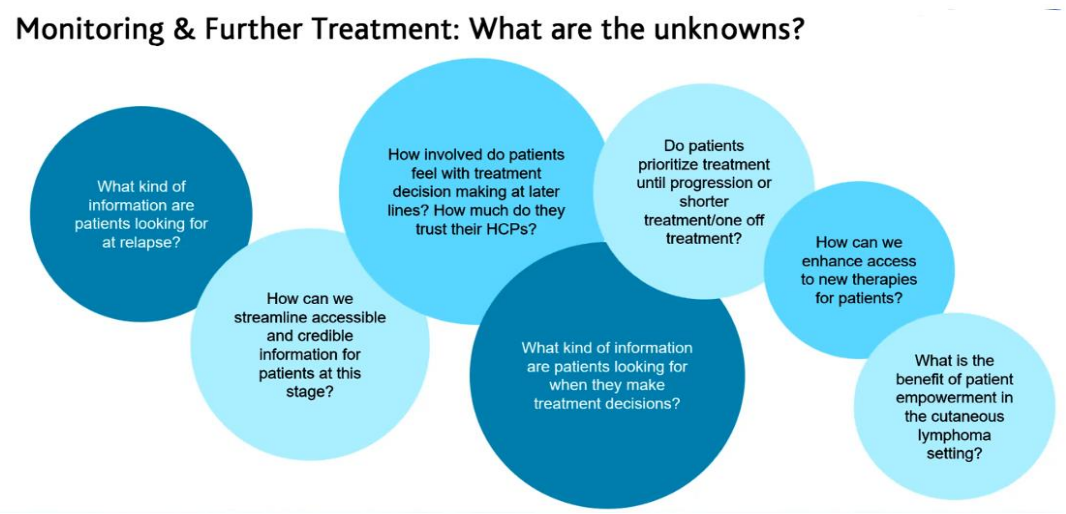
Treatment Pathways



Monitoring & Further Treatment: What are the unknowns?

What kind of information are patients looking for at relapse?

How can we streamline accessible and credible information for patients at this stage?

How involved do patients feel with treatment decision making at later lines? How much do they trust their HCPs?

What kind of information are patients looking for when they make treatment decisions?

Do patients prioritize treatment until progression or shorter treatment/one off treatment?

How can we enhance access to new therapies for patients?

What is the benefit of patient empowerment in the cutaneous lymphoma setting?

The journey, both to and from, the hospital for treatment is very demanding on the patient, particularly in cases where patients have been living with the disease for an extended period.

For example:

- In France, as soon as a patient is diagnosed with cancer, all costs are covered. However, for patients living with cutaneous lymphoma, several topical treatments do not qualify for reimbursement, with extra costs often mounting up for patients.
- In the Netherlands, costs are covered at diagnosis, however, the available options are not clear, nor are they discussed by physicians. This contributes to psychological issues about patient outcomes.

Treatment pathways for patient with cutaneous lymphoma are different from many other lymphoma treatments, presenting specific challenges. For instance, cutaneous lymphoma is, for most people, a chronic, continuous condition. Further, while treatment approaches tend to be personalized, there are unknowns in longer-term treatment plans that are dependent on the individual and their respective disease course. The importance of having an expert physician knowledgeable about the challenges, as well as an understanding of the available options, is essential.

For example:

- In the Netherlands there is a leading expert centre for cutaneous lymphoma. Disease information, as well as information about treatment options, is made available to patients in the region.

WHAT WE HEARD FROM COMMUNITY ADVISORY BOARD MEMBERS	
💬	Treatment planning in a specialist clinical setting was viewed as a benefit. A CAB member spoke of the dialogue they had with the care team. The patient had no real expertise on their treatment, they needed to trust the experts fully. A high level of communication and collaboration by the treatment team helped to ensure the patient had access to information, as well as sufficient time to consider treatment approaches.
💬	The need to trust in the knowledge of doctors was also expressed by a CAB member who indicated that although they did not have many treatment options, the doctor communicated the different options, what they planned to do, and how their treatment will proceed.
💬	Facing a chronic condition has an ongoing impact on quality of life; it is a constant balance between treatment which can make your feel poorly and dealing with the ups and downs of the tumours.
💬	When choosing treatments, the capacity to continue as normal life as possible is important because cutaneous lymphoma is a long journey.
💬	The stigma around the psychological impacts of the condition and needing help to cope or manage is something that isn't talked about enough.
💬	A CAB member said they continue to feel very alone because they struggle with how to explain their cancer and its chronic nature to their friends, family, and others.

PROSPER Study

Angela Williams, Health Economics and Outcomes Research Lead with Kyowa Kirin spoke to the Prospective Research based Observational Study of Poteligeo Experience in the Real-World, also known as PROSPER.

PROSPER, a real-world study based in clinical practice, is intended to build on the randomised controlled trial evidence of treatment benefit and describe patient-reported change in signs and symptoms of disease, as well as implement a HRQL following initiation of treatment with mogamulizumab in real-world clinical practice. Additionally, the PROSPER study aims to gather insight into carer/spouse-related change in carer burden, as well as insight into treatment patterns in real-world clinical practice and associated patient-reported outcomes.

Telephone interviews with patients were conducted by Kyowa Kirin with insights helping to inform a proposed data collection schedule while under treatment. The study trial will continue during the duration of treatment (+/- six months) to help capture was how long the benefit remained post-treatment. Eight weeks after ceasing treatment, patients will be asked to answer the questions again, and to learn if no new systemic treatment has been stated after 16-weeks. Further, for carers, data collection uses the CarGOQoL (Caregiver Oncology Quality of Life) Questionnaire.

Additionally, the PROSPER study measures the quality-of-life aspect and, developed by collaborating with patients, included questions to help measure psychological and social impacts to take into consideration that cutaneous lymphoma is a highly visible disease Further, interviews with patients and carers or spouses will be conducted both at baseline and six months later.[v] (Note: A copy of the questionnaire may be shared by Kyowa Kirin.)

WHAT WE HEARD FROM KYOWA KIRIN	
💬	Capturing the reasons for the discontinuation of treatment requires the need to strike the right balance in the level of detail in the questions, which will help properly interpret the responses.
💬	Participation in the study will be limited to countries where mogamulizumab is/was reimbursed. The goal is to recruit eighty participants naïve to mogamulizumab in total: twenty in North America, and sixty in Europe in six countries . (Please note, the identification of centres is a work in progress.)

WHAT WE HEARD FROM COMMUNITY ADVISORY BOARD MEMBERS	
💬	Relaying information regarding daily health or weekly changes is important when visiting with doctors. However, it can be challenging at times for patients to recall details about physical symptoms. To ensure details are not missed or overlooked, an app would be valuable tool for patients to record information. To simplify this process while limiting the time commitment patients are expected to invest, the option to select from an icon may be considered.
💬	When studies contain scales, it is important to ensure questions are clearly defined, as they may be confusing and/or unnecessarily duplicate other questions. Additionally, there is value in looking at rash from treatment as opposed to rash from the disease as this may further support how data is captured, how data would be used, and how data will be reported on.
💬	Should include side effects as reported by the patient, not just those physicians think are important to be measured. This will help ensure that patients feel their input is valuable and not a waste of their time. It is particularly important for people to see what is being captured with the questions, and why.
💬	With respect to studies, a representative sample of the population may not be seen where clinical trials have been previously offered in centres due to doctors having a greater understanding about the drug and cutaneous lymphoma. When seeking real-world data, doctors that do not have the same level of expertise might be preferrable, offering an opportunity to expand access and reach a more representative sample of the population.
💬	Limiting to a small number of countries may not produce a good overall picture given the huge variability in clinical practice. For example, measurement of the emotional impact may be influenced by in-country access to supportive services.

Summary

Patients, patient advocates, and members of patient organisations provide interesting insights, additional context, and valuable first-hand experiences that often bridge gaps and help to inform the manufacturing of medicines that make a measurable difference in the lives of patients.

Important considerations and insights include:

- the psychology of the disease, and the impact on the person affected in addition to family, friends, and employers;
- impact of adverse events of treatments on quality of life is especially important in a chronic condition;
- the reach and power – both positive and negative – of patients conducting research themselves to better understand their symptoms, diagnosis, and treatment;
- there are key actionable items in areas where patient care, communication, and outcomes might be improved.

The patient experience for those diagnosed with cutaneous lymphoma is not a linear pathway. Rather, misdiagnosis is common as symptoms often present to doctors as a simple skin condition, with the focus of clinicians tending to remain at the single site, rather than considering that it may be a systemic problem. Inevitably, this leads to a loss of time before diagnosis occurs. Patients in the pre-diagnosis phase of their cutaneous lymphoma tend to encounter a lack of information to varying degrees. This extended diagnosis process can have a considerable negative effect on patients. Doctors are often not widely aware of cutaneous lymphoma and therefore, diagnosis is frequently late. This may be further compounded by the lack of specialists able to treat cases that are accurately diagnosed.

At all stages, transparent and effective communication between patient and doctor is paramount. Doctors may not adequately inform their patient that the diagnosis is a form of cancer during communication, contributing to psychological repercussions and fears when a rare cancer diagnosis is understood. This lack of transparent communication may have more serious implications for patients as a lack of communication between patient and doctor can adversely impact the relationship and erode the level of trust. Credible information is essential for patients to help them understand their cancer and the chronic nature of care. Patients may turn to other sources, or conduct their own research, when they do not get satisfactory information from their care team, presenting additional challenges with accuracy of information and management of fears.

Pertaining to the disclosure of a diagnosis of cutaneous lymphoma in the workplace, patients may elect to refrain from sharing with employers due to the fear it might negatively impact their employment. Patients may also experience challenges in sharing information with their family members or close friends. Psychological support is needed to help patients process and communicate with others the nature of their cancer. While few mentioned they had access to this type of support through their care team, they spoke of how helpful patient organisations are in providing different types of support to address these issues, as well as good information on the cancer itself.

Treatment pathways for patient with cutaneous lymphoma differs from other lymphoma treatments and as such, present specific challenges. For instance, cutaneous lymphoma is, for most people, not curable and instead is a chronic, continuous condition. Further, while treatment approaches tend to be personalized for patients, there are unknowns in longer-term treatment plans that are dependent on the individual and their respective disease course. The importance of having a doctor with expertise and knowledgeable about the challenges and available treatment options is essential, though not available to all.

It is important that real-world studies - such as the Prospective Research based Observational Study of Poteligeo Experience in the Real-World (PROSPER), a study based in clinical practice – ensure representative samples. For instance, a representative sample of the population may not be reasonable in centres where clinical trials have been previously offered. This may be due to doctors having a greater understanding about the drug and cutaneous lymphoma. When seeking real-world data, doctors that do not have the same level of expertise might be preferrable, offering an opportunity to expand access and reach a more representative sample of the population. Patients are willing to participate in studies like this, even if the expectations are many, as long as the impact is demonstrable and communication pathways exist for them to see how their participation benefitted care.

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