Montréal

6TH World Congress of Cutaneous Lymphomas

JUNE 25-27, 2026

2026 Abstracts

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SESSION 1A: NEW BIOMARKERS FOR PREDICTING OUTCOME IN CTCL

1A.01 Evaluation of TRBC1 Immunohistochemistry Versus High-Throughput Sequencing of TCRB Gene for Clonality Assessment in Cutaneous T-Cell Lymphomas

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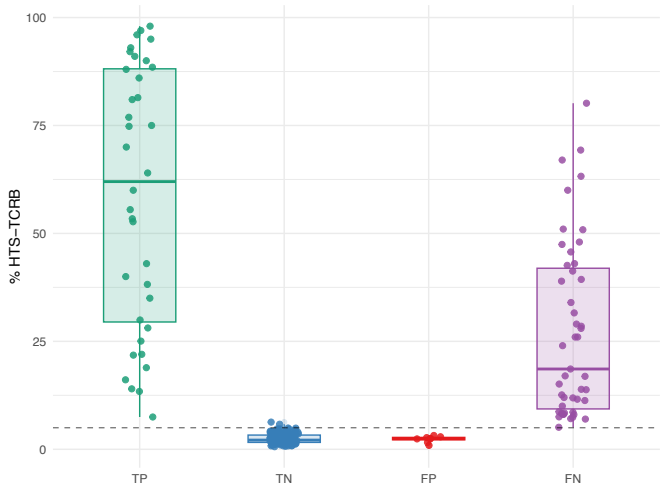
Introduction: Diagnosis of CTCL remains challenging. The use of high-throughput sequencing (HTS) of *TCRB* gene for clone detection is highly sensitive but limited by cost and availability. TRBC1 immunohistochemistry (IHC) has emerged as a potential surrogate, yet its diagnostic performance remains unclear versus HTS-TCRB.

Methods, Results: We conducted a single-center prospective diagnostic accuracy study assessing the performance of TRBC1 IHC for T-cell clone detection in skin biopsies submitted for suspected CTCL. All samples underwent sequential CD3 and TRBC1 IHC staining. TRBC1 quantitative scoring was performed both on the entire $CD3^+$ T-cell population (TRBC1+/CD3) and on morphologically suspicious $CD3^+$ cells (TRBC1+/susp). Performance was stratified by infiltrate density, localization and clinical context. HTS-TCRB result served as reference (clonality was considered when TCF>5% and RPF >3.7). Diagnostic performance was quantified using ROC curve analysis.

Among 234 prospectively included biopsies, all had TRBC1/CD3 staining and 229 had informative HTS-TCRB result. Using symmetrical cut-offs obtained from ROC/Youden optimization, TRBC1+/CD3 percentage (<17.5% or >82.5%) showed an AUC of 0.71, with 43% sensitivity and 94% specificity. Diagnostic performance varied with infiltrate density (abundant, AUC=0.75; moderate, 0.72; weak, 0.65). Quantification of TRBC1+/susp showed equivalent performance (AUC=0.73, sensitivity 64%, specificity 76%). Accuracy for TRBC1+/susp in epidermis (n=145) was 67%, while it reached 100% in the dermis (n=14) and the follicle (=6). Across clinical contexts, TRBC1+/CD3 performance was lowest in the context of "mogamulizumab-associated rash versus CTCL" (AUC=0.53; accuracy= 57%). Using TRBC1+/CD3 cut-offs (<17.5% or >82.5%), false positives were rare (4%, 7/202, median HTS-TCRB% 2.5%), while false negatives represented 23% of total cases (47/202; median 18.6%); true positives showed markedly higher clonality (median 62%) (figure 1).



HTS–TCRB result (tumor clone frequency, TCF) is plotted according to the TRBC1/CD3 IHC result: true positive (TP: IHC predicts clonality and HTS detects a significant clone), true negative (TN: IHC predicts no clonality and HTS detects no significant clone), false positive (FP: IHC predicts clonality but HTS detects no significant clone), false negative (FN: IHC predicts no clonality but HTS detects a significant clone). Each dot is one biopsy.

Conclusion: TRBC1 immunohistochemistry provides a rapid and accessible surrogate for T-cell clonality assessment. Its diagnostic performance compared with HTS-TCRB supports integrating TRBC1 into routine CTCL diagnostic workflows.

Learning Objectives:

- TRBC1 immunohistochemistry diagnostic performance compared with HTS-TCRB for detecting T-cell clonality in CTCL skin biopsies.
- Potential Integration of TRBC1 immunohistochemistry using symmetrical identified cut-offs to detect T-cell clonality in routine dermatopathology practice.

1A.02 Unraveling the Nature of T-Cell Clones of Uncertain Significance in Cutaneous T-Cell Lymphomas

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Introduction: T-cell receptor (TCR) sequencing is increasingly incorporated into the diagnosis and monitoring of cutaneous T-cell lymphomas (CTCL). However, interpretation is often confounded by multiple dominant TCR clonotypes, whose etiology remains poorly understood. We aimed to determine the incidence of multiple dominant clonotypes through serial TCR high-throughput sequencing (TCR-HTS), immunophenotypically and genetically characterize these dominant T-cell populations, and assess their clonal relationship to CTCL.

Methods, Results: We reviewed 2065 samples (blood n=948, skin n=1091, other n=26) from 271 CTCL patients (MF n=211, SS n=60)

sequenced using the clonoSEQ® platform from 2012–2023 (median 6 samples/patient). Dominant productive TCR clonotypes were included, as defined by clonoSEQ® criteria, and clonotypes with identical VDJ rearrangements were excluded. Among patients with an emerging second dominant productive TCRβ clonotype, 11 had cryopreserved PBMCs available. These, and PBMCs from 10 age-matched healthy donors underwent TCR-HTS using the LymphoTrack® assay. Multiparametric spectral flow cytometry (MFC), FACS sorting, whole-exome sequencing (WES), and hybrid-capture TCR sequencing were performed.

Among 245 CTCL patients, 95 (39%) had ≥2 unique dominant productive TCRβ clonotypes, and 31 (13%) had ≥3. An alternative platform confirmed a high-frequency clonotype (>3%) in all 11 CTCL PBMC samples and in none of 10 healthy donors. MFC identified ≥1 clonal T-cell population per patient, variably expressing CD4 and CD8, predominantly with a terminal effector phenotype (CD45RA+, CD56+, CD57+), consistent with T-cell clones of uncertain significance (T-CUS). T-CUS harbored fewer somatic variants than CTCL biopsies but more than polyclonal T cells, comparable mutational burden to single-cell-derived normal T-cell colonies, and no shared variants with matched CTCL. However, T-CUS harbored nonsynonymous variants in CTCL-/cancer-associated genes. STAT3/STAT5B variants, unexplained cytopenias, and UV-associated mutational signatures were absent.

Conclusion: Emerging dominant TCR clonotypes are common in CTCL and often arise within fluctuating T-CUS populations in blood and skin. These appear clonally unrelated to CTCL.

Learning Objectives:

- Recognize that multiple dominant productive TCRβ clonotypes are common in CTCL.
- Identify the immunophenotypic and genomic features of T-cell clones of uncertain significance in CTCL.
- Interpret emerging dominant TCR clonotypes in CTCL in the context of possible clonally unrelated T-CUS rather than disease progression.

1A.03 The Genomic Landscape of Mycosis Fungoides: Therapy-Associated UV Mutagenesis and Oncogenic JUNB A282V Mutation

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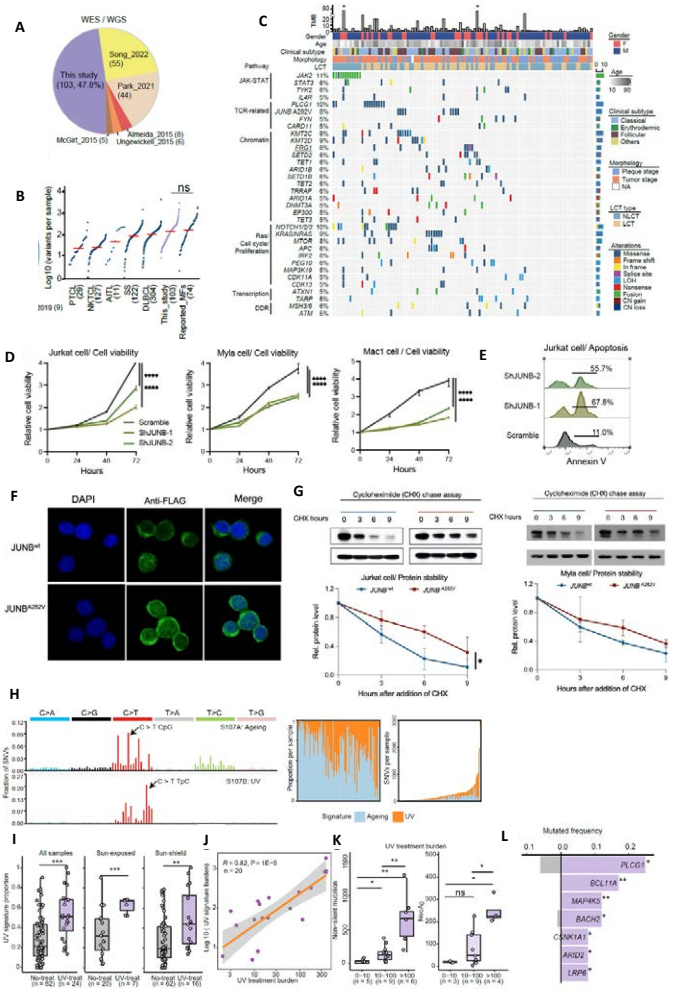
Introduction: Mycosis fungoides (MF) is a heterogeneous cutaneous T-cell lymphoma with an incomplete genomic characterization.

Methods, Results: We performed comprehensive genomic profiling of 103 MF patients (Figure 1A). Notably, our cohort's tumor mutational burden (TMB) was comparable to previously reported MF samples (Figure 1B). Through this large-scale analysis, we identified 37 driver genes enriched in JAK/STAT (e.g., *JAK2* fusions, 11%), T-cell function (*PLCG1*, 10%; *JUNB*, 8%), and epigenetic regulation (Figure 1C). Functional assays revealed that *JUNB* is a potent oncogene; its knockdown triggered increased apoptosis, and reduced viability in CTCL cell lines (Figure 1D-E). Notably, the recurrent *JUNB* ^{A282V} mutation conferred a superior growth advantage over wild-type *JUNB* (Figure 1F). While A282V did not alter nuclear localization or mRNA expression, protein stability assays (CHX chase) demonstrated that the A282V mutant significantly increased protein half-life, thereby enhancing its oncogenic effect (Figure 1G).

Integrated analysis revealed aging- and UV-associated signatures as dominant mutational processes (Figure 1H). UV signatures were significantly enriched in patients with prior therapeutic UV exposure, regardless of biopsy site (Figure 1I). In patients treated with narrow-band UVB (NB-UVB), the UV signature weight correlated strongly with cumulative treatment load (R=0.82, P=1.0×10^{-5}, Figure 1J). Increased UVB exposure was associated with higher non-synonymous mutation burdens, predicted neoantigens, and an increased frequency of mutations in key pathways (e.g., *PLCG1*), indicating therapy-driven mutagenesis (Figure 1K-L).



Conclusion: This study establishes a large-scale genomic map of MF. Our findings highlight therapy-associated UV mutagenesis as a significant contributor to genomic evolution in MF, providing a framework for molecular stratification and future functional exploration of recurrent mutations like *JUNB* ^{A282V}.

Learning Objectives:

1. Describe the key genomic drivers and mutational processes in Mycosis Fungoides (MF);
2. Discuss the oncogenic mechanism of the recurrent *JUNB* ^{A282V} mutation;
3. Evaluate the association between therapeutic UV exposure and genomic evolution in MF, including its link to increased mutation burden and potential neoantigens.

1A.04 Distinct Molecular Signatures as Predictors of Early Mortality in Advanced Mycosis Fungoides

Rebollo-González, Marcos[1], Rodríguez, Marta[1], Moreno-Vílchez, Carlos[2], Torre-Castro, Juan[1], Moreno-Delgado, María[1], Gotor-Rivera, Alfonso[3], Climent, Fina[2], Muniesa, Cristina[2], Servitje, Octavio[2], Díaz de la Pinta, Francisco Javier[1], Rodríguez-Peralto, José Luis[3], Manso, Rebeca[1], Rodríguez-Pinilla, Socorro María[1], Ortiz-Romero, Pablo L.[3]

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Introduction: MF progresses from early to advanced stages. While median survival in advanced-MF is 4-5 years, a clinically unfavourable-subgroup progresses rapidly (OS<2 years). Biomarkers related to early-mortality in advanced-MF are poorly known. This study aims to identify molecular markers of rapid-progression and potential therapeutic-targets, enabling early-identification of high-risk patients, who may benefit from personalized trial-based therapy.

Methods, Results: Forty-one tumour-stage MF-patients (median:OS-25 months, range:1–57) were stratified by survival: <24 months (n=10); ≥24 months (n=31). DGE was assessed using a custom NanoString panel of 93 genes, with statistical-significance set at adjusted p<0.05. Tumour microenvironment (TME) composition was inferred through transcriptomic deconvolution using CIBERSORTx. An independent cohort of 18 tumour-stage MF-patients (<24 months, n=7; ≥24 months, n=11) was analysed to validate the reproducibility of the findings. Clinical variables are still collected to assed the IPI score and its interrelationship to our biological model.

Distinct molecular and immune signatures were identified between survival groups. Patients with survival ≥24 months showed enrichment of interleukin-4/interleukin-13 and BCR-signalling, innate-immunity, and platelet-activation pathways, with TME enriched in resting T-CD4 naïve cells, M2-macrophages, mast-cells resting and eosinophils. In contrast, patients with survival <24 months exhibited enhanced TCR-signalling, CD28 co-stimulation, G-protein–coupled receptor and tyrosine-kinase signalling, with TME dominated by CD8+ T-cells, T-CD4 memory resting and dendritic-cells resting. Gene expression analysis revealed upregulation of *EGR2* and *RORC* in the better-prognosis group and *IL-10*, *IKZF2*, *PRKACB*, *CD3D*, *CD3E*, *CD3G* in the poor-prognosis group. These findings were validated in an independent cohort. Full follow-up OS-analyses showed *EGR2* (p=0.0029), *RORC* (p=0.0006) associated with longer survival, while *IKZF2* (p=0.0357), *IL-10* (p=0.0266), *PRKACB* (p=0.0309), *CD3E* (p=0.0171), *CD3G* (p=0.0207) predicted poor prognosis and early-disease-associated mortality.

Conclusion: Our findings reveal molecular and immune signatures associated with prognosis in tumour-stage-MF patients. *IL-10*, *IKZF2* and *PRKACB* may predict early-mortality, and represent potentially druggable targets that could prolong OS in high-risk MF-tumoral-stage-patients.

Learning Objectives:

- Explain how distinct molecular and tumour microenvironment signatures correlate with early mortality in tumour-stage mycosis fungoides and their relevance in patient stratification.
- Recognize the prognostic significance of IL10, IKZF2, and PRKACB gene expression and how these biomarkers can inform risk-adapted therapeutic strategies in cutaneous lymphoma.
- Discuss translational opportunities for integrating molecular profiling into clinical management pathways for high-risk tumour-stage mycosis fungoides patients.

1A.05 Head and Neck Lesions as Sentinel Clinical Features of Dupilumab-Associated Cutaneous T Cell Lymphoma

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Introduction: Dupilumab has fundamentally altered the therapeutic landscape for moderate-to-severe atopic dermatitis (AD). Despite its favorable safety profile, accumulating case reports and recent database analyses consistently indicate an elevated risk of cutaneous T-cell lymphoma (CTCL). Given the current inability to predict individual deterioration after dupilumab, identifying clinical signs enabling earlier recognition of dupilumab-associated CTCL is urgently needed.

Methods, Results: This retrospective cohort study was conducted using data from the Skin Lymphoma Clinic of Peking University First Hospital from 2020 to 2025. Participants included patients with histopathologically confirmed CTCL who had received dupilumab therapy prior to lymphoma diagnosis. Clinical characteristics, timeline of dupilumab exposure, and molecular features of skin lesions analyzed via single-cell RNA sequencing (scRNA-seq).

A total of 26 patients were included (median age at CTCL diagnosis, 47 years [range, 20-83 years]). The median duration of dupilumab therapy was 3 months (range, 1-15 months), and the median interval from dupilumab initiation to CTCL diagnosis was 7 months (range, 1.5-41 years). This cohort demonstrated a remarkable predominance of head and neck involvement (80.8%, 21 patients) and frequent histopathologic folliculotropism (50%, 13 patients) at diagnosis. A systematic review of published literature revealed that 52.6% of patients developed new or progressive head and neck lesions following dupilumab therapy. Integrated scRNA-seq analysis revealed shared molecular drivers contributing to the specific head and neck phenotype between DAHND and folliculotropic mycosis fungoides (FMF).

Conclusion: The predilection for head and neck involvement in dupilumab-associated CTCL, coupled with immunologic overlap between DAHND and FMF, underscores head and neck lesions as key clinical indicators of dupilumab-associated CTCL.

Learning Objectives: The emergence of new or worsening head and neck lesions serves as a critical sentinel sign of underlying CTCL unmasked by dupilumab. Clinicians should maintain high suspicion for CTCL when atopic dermatitis patients develop new or worsening head and neck lesions during or after dupilumab therapy.

1A.06 Dupilumab Accelerates T-Cell Lymphoma via A20-Deficient NF-kB Signaling and STAT3/5 Amplification

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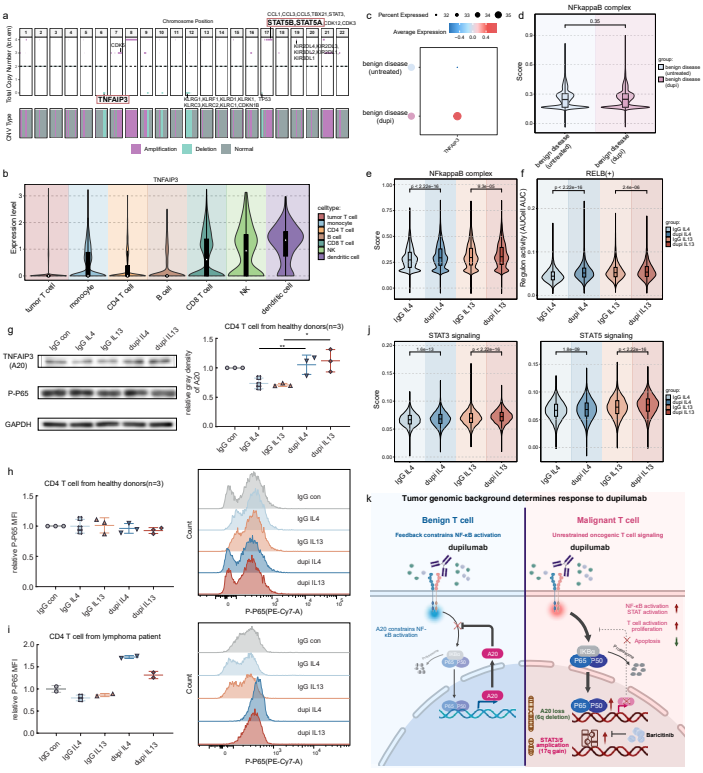
Introduction: Dupilumab, an IL-4Rα–blocking antibody, is widely used for atopic dermatitis, yet paradoxical acceleration of cutaneous T-cell lymphoma has been reported in rare cases. The tumor-intrinsic mechanisms underlying this adverse response remain poorly defined.

Methods, Results: We investigated a patient with CD4+ γδ T-cell lymphoma that progressed dramatically after dupilumab treatment. Peripheral blood mononuclear cells were cultured *ex vivo* under type 2 inflammatory conditions with or without dupilumab, and analyzed by single-cell RNA sequencing (scRNA-seq). Despite effective suppression of type 2 signaling, dupilumab consistently increased the relative abundance of malignant γδ T cells, enhanced proliferative activity, and upregulated anti-apoptotic programs.

To define the molecular basis of this response, integrated whole-genome sequencing was performed. This revealed loss of *TNFAIP3* (A20) due to chromosome 6q deletion, together with amplification of *STAT3* and *STAT5* on chromosome 17. Loss of A20 removed a critical negative-feedback brake on NF-κB signaling, permitting dupilumab-induced cytokine perturbation to amplify NF-κB activity. Accordingly, scRNA-seq analyses demonstrated selective upregulation of NF-κB signaling and NF-κB–dependent survival programs in tumor cells, a pattern not observed in inflammatory controls.

Mechanistic in vitro assays further supported this model. In CD4+ T cells from healthy donors, type 2 cytokine blockade induced A20 expression and constrained NF-κB activation. In contrast, patient-derived T cells exhibited intrinsically low A20 expression and exaggerated NF-κB activation, including increased p65 phosphorylation, following dupilumab exposure. Concurrent STAT3/5 amplification provided an additional oncogenic signaling axis. Based on these findings, the patient was treated with the JAK inhibitor baricitinib, resulting in rapid tumor burden reduction and marked clinical improvement.



Conclusion: This case illustrates how tumor intrinsic genomic alterations can repurpose cytokine blockade into a tumor-promoting signal, revealing both a mechanism of dupilumab-associated lymphoma progression and a therapeutic vulnerability.

Learning Objectives:

1. Recognize that paradoxical progression of cutaneous T-cell lymphoma during dupilumab therapy is rare but can occur in the presence of specific tumor-intrinsic genomic alterations.
2. Explain how loss of *TNFAIP3* (A20) disrupts NF-κB negative feedback and enables IL-4Rα blockade to amplify NF-κB–dependent survival signaling in malignant T cells.
3. Apply genomic and molecular features, including aberrant NF-κB and JAK–STAT signaling, to inform risk assessment and therapeutic decision-making in patients with suspected or confirmed T-cell lymphoma receiving cytokine-targeted therapies.

1A.07 Loss of Fibroblast Interaction with Malignant T-Cell Clones is Associated with Aggressive Ctcl Behavior Across CD4+, CD8+ and TCR-γδ+ Malignant Phenotypes

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Introduction: Cutaneous T-cell lymphomas (CTCL) span a broad clinical spectrum ranging from self-limited to aggressive variants, however, the mechanisms underlying these divergent clinical behaviors remain insufficiently characterized.

Methods, Results: Using single-cell RNA sequencing, we profiled skin samples from self-limited, spontaneously regressing lymphomatoid papulosis (LyP) cases with CD4+, TCR-γδ+ or CD8+ clonal phenotypes and compared them with corresponding cases of aggressive, advanced-stage CTCL, including CD4+ or TCR-γδ+ mycosis fungoides (MF) and CD8+ aggressive epidermotropic CTCL. CellChat analyses demonstrated higher interaction scores across all skin cell populations in LyP compared to advanced-stage CTCL. These elevated interaction scores in LyP were driven by crosstalk between fibroblasts and malignant T-cells, namely *CCN5*+*SLPI*+ secretory-reticular as well as *CXCL2*+*APOE*+*CCL19*+ pro-inflammatory fibroblasts. Components of this interaction included the CXCL12-CXCR4 axis, as well as type I and type VI collagen with CD44, both of which can enhance homeostatic tissue retention and appear to be markedly decreased in aggressive CTCL compared to LyP. In parallel, expression of *THEMIS*, a critical regulator of T-cell activation and effector functions, was lost across all CD4+, CD8+, and TCR-γδ+ malignant clones of advanced-stage CTCL subtypes, whereas expression was preserved in all LyP samples.

Conclusion: Taken together, these findings suggest that loss of stromal tissue control over malignant T-cell clones is likely a key contributor to the distinct clinical behaviors observed between LyP and advanced-stage CTCL. Furthermore, this study identifies mediators associated with self-limited versus aggressive CTCL behavior, which may inform future immunomodulatory treatment strategies.

Learning Objectives:

1. To understand how stromal-immune interactions contribute to self-limited versus aggressive behavior in cutaneous T-cell lymphomas
2. To identify molecular mediators associated with self-limited versus aggressive cutaneous T-cell lymphoma behavior

SESSION 1B: FROM NOVEL TOPICALS TO REAL-WORLD OUTCOMES

1B.01 WITHDRAWN

1B.02 A Pilot Study to Assess Safety and Efficacy of Tofacitinib 2% Cream in the Treatment of Early-stage Mycosis Fungoides

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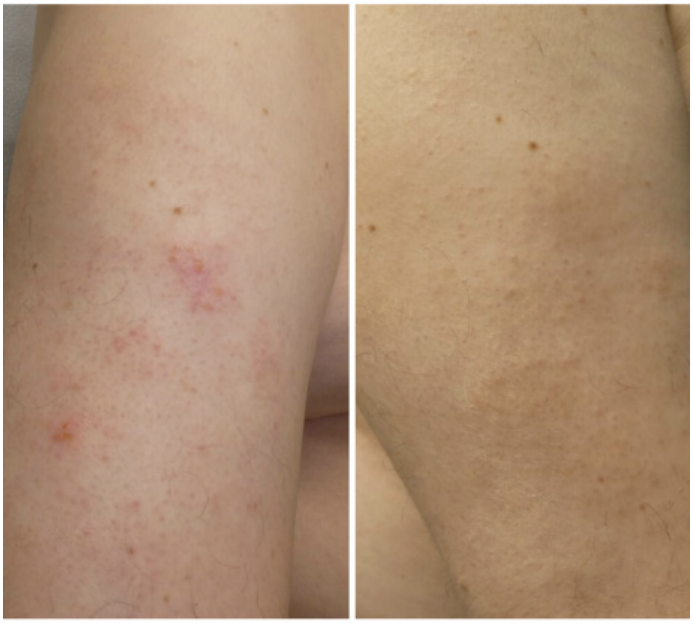
Introduction: Introduction: There is mounting preclinical evidence to suggest that deregulation of Janus kinase/signal transducer and activator of transcription (JAK/STAT) signaling is implicated in the pathogenesis of mycosis fungoides (MF). We investigated tofacitinib 2% cream, a selective inhibitor of JAK1 and JAK3, because of the specific role of STAT5 activation through JAK1 and JAK3 in early-stage MF.

Methods, Results: In this single-center pilot study, patients with MF stage IA-IIA applied tofacitinib 2% cream twice daily to up to 5 index lesions. The primary endpoint was index lesion response rate, defined as 50% or greater improvement in modified Composite Assessment of Index Lesion Severity (mCAILS) score from baseline after 12 weeks of therapy. Paired skin biopsies at weeks 0 and 4 were collected for explorative correlative studies.

To date, 6 patients have undergone treatment with tofacitinib 2% cream, including 3 patients with data available for endpoint analysis after completing 12 weeks of therapy. Treated lesions achieved 50% or greater improvement from baseline in 2 of 3 evaluable patients. Figure 1 highlights clinical response in a representative patient with folliculotropic MF at baseline (left) and after 12 weeks of treatment (right). One patient demonstrated improvement but did not reach criteria for partial response. Treatment with tofacitinib 2% cream was well-tolerated, and there were no serious adverse effects nor were there adverse effects suspected to be related to study drug.



Conclusion: Preliminary results from this pilot study suggest tofacitinib 2% cream has favorable tolerability. Encouraging response data supports ongoing enrollment with a goal of 20 patients to better define its efficacy in early-stage MF.

Learning Objectives:

1. To understand the mechanism of Janus kinase/signal transducer and activator of transcription (JAK/STAT) signaling and its implications in the pathogenesis of early-stage mycosis fungoides (MF)
2. To understand the potential role of topical JAK/STAT inhibition as a tool in the treatment arsenal of patients with early-stage MF

1B.03 Treatment Outcomes and Frequent Relapsers in Primary Cutaneous Indolent B-Cell Lymphomas: A 213-Patient Single-Center Cohort Study

Alberti-Violetti, Silvia[1,2], Rampi, Nicolò[3], Simeoli, Domenico[2], Colombo, Riccardo[3], Croci, Giorgio[4,1], Bosi, Alessandro[3], Rossi, Francesca G.[3], Venegoni, Luigia[1], Zamprogno, Marzia[2], Merlo, Valentina[2], Marzano, Angelo V.[1,2], Onida, Francesco[5,1], Passamonti, Francesco[1,3], Merli, Michele[3], Berti, Emilio F.[6]

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Introduction: Primary cutaneous follicle center lymphoma (PC-FCL) and marginal zone lymphoma (PC-MZL) exhibit excellent survival but high relapse rates. Optimal prognostic stratification and treatment selection, particularly regarding time-to-next-treatment (TTNT), remain incompletely defined.

Methods, Results: We retrospectively analyzed 213 consecutive patients with PC-FCL (n=112, 52.6%) or PC-MZL (n=101, 47.4%) treated at a single Italian referral center (1990–2025). Median age was 54.1 years; median follow-up 78 months (range, 6–424). Univariate Cox regression and Fine-Gray competing risk models evaluated associations with relapse-free survival (RFS) and TTNT. Frequent relapsers were defined as patients experiencing ≥2 relapses.

Five-year OS was 93%; 26 patients died (12.2%), 8 (3.7%) from lymphoma-related causes. Relapses occurred in 142 patients (66.7%); 101 (47.4%) were frequent relapsers. Median TTNT was 40 months (range, 0–325). Factors associated with shorter RFS included T stage (T3 vs T1: HR=2.46, p=0.006), lower limb involvement (HR=2.40, p=0.011), age (HR=1.03/year, p=0.001), beta-2 microglobulin (HR=1.46, p<0.001), LDH (HR=1.002, p=0.027), and IgM (HR=1.34, p=0.023). Histology did not predict RFS (p=0.086). Radiotherapy was associated with longer TTNT versus surgery and topical corticosteroids (p=0.015). Chest wall location predicted shorter TTNT (HR=1.87, p=0.024). Frequent relapsers exhibited reduced TTNT (12 vs 61 months, p<0.001) but preserved OS. Frequent relapser status was associated with younger age (OR=0.98/year, p=0.014) and PC-MZL histology (OR=1.85, p=0.026), but not with T stage or treatment modality.

First-line treatment	N (%)	Median TTNT, months (range)
Radiotherapy	106 (49.8)	54 (1–312)
Topical corticosteroids	50 (23.5)	20 (0–325)
Surgery	43 (20.2)	25 (0–319)
Rituximab-based	6 (2.8)	59 (6–181)
Other	8 (3.8)	22 (5–148)

Table 1. First-line treatment modalities and time-to-next-treatment (TTNT) in our cohort

Conclusion: Radiotherapy was associated with longer treatment-free intervals. Anatomic site and serum biomarkers warrant further evaluation for risk stratification. Nearly half of patients became frequent relapsers—a subset associated with PC-MZL and younger age but not with lesion burden. Preserved OS suggests an intrinsic relapsing phenotype, supporting molecular characterization over systemic therapy intensification.

Learning Objectives:

1. Recognize clinical and laboratory factors associated with shorter relapse-free survival in primary cutaneous indolent B-cell lymphomas, including T stage, anatomic site (lower limbs, chest wall), age, and serum biomarkers (beta-2 microglobulin, LDH, IgM), which may inform risk stratification beyond traditional staging.
2. Recognize that radiotherapy was associated with longer time-to-next-treatment compared to other therapies; rituximab-based regimens are underrepresented due to the extended temporal span of the cohort, limiting direct comparison.
3. Understand that frequent relapsers (≥2 relapses) represent a distinct subset associated with PC-MZL histology and younger age, but with preserved overall survival, suggesting the need for molecular characterization rather than routine systemic therapy intensification.

1B.04 Folliculotropism and Infection-Associated Outcomes in Cutaneous T-Cell Lymphoma

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Introduction: Infections are a major source of morbidity and mortality in cutaneous T-cell lymphoma (CTCL). While advanced stage and immunosuppression are recognized risk factors, the contribution of folliculotropism to infection susceptibility and survival outcomes remains poorly defined.

Methods, Results: In this retrospective observational cohort study, adult patients with CTCL were identified from institutional databases. Infection history was categorized by timing relative to CTCL diagnosis, organism type, severity, and source. Associations between folliculotropic mycosis fungoides (FMF) and infection outcomes were evaluated using Firth penalized logistic regression. Overall survival was analysed using Firth penalized Cox proportional hazards models.

Overall, 43% of the entire CTCL cohort experienced at least one documented infection. Post-CTCL diagnosis infections were more frequent among patients with FMF (27/59) than non-FMF (18/78) (46% vs 23%; p= 0.006). In adjusted analyses for age, sex, and late stage at diagnosis, folliculotropism was associated with increased odds of any infection ever (OR 2.58, 95% CI 1.23-5.57; p=0.012) and post-CTCL diagnosis infection (OR 3.38, 95% CI 1.53-7.85; p=0.002), but not with organism-specific or clinical severity of infections. In survival analyses, multiple infection phenotypes were associated with increased mortality, including any infection, bacterial infections, severe infections, skin-origin infections, and post-diagnosis S. aureus infections. Interaction testing showed little evidence that these infection–mortality associations differed by FMF status (interaction p>0.05 for all phenotypes except skin-origin infections), suggesting that the adverse prognostic impact of infections is broadly similar in FMF and non-FMF CTCL.

Conclusion: In CTCL, folliculotropism is associated with increased infection susceptibility, but infection-associated mortality does not differ meaningfully between folliculotropic and non-folliculotropic disease. Instead, survival outcomes are driven by specific high-risk infection phenotypes rather than CTCL subtype or overall infection burden.

Learning Objectives:

1. Describe the relationship between folliculotropism and infection susceptibility in cutaneous T-cell lymphoma.
2. Identify infection phenotypes associated with increased mortality in patients with cutaneous T-cell lymphoma.
3. Recognize the prognostic value of infection severity and tissue origin beyond CTCL subtype and stage.

1B.05 The Risk of Developing Second Primary Malignancies in Patients with Cutaneous Lymphomas

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Introduction: Patients with cutaneous T-cell lymphomas (CTCL) have an increased risk of developing certain second primary malignancies. However, the risk of developing other second primary malignancies in patients with primary cutaneous B-cell lymphomas (pCBCL) and the risk of keratinocyte malignancies in patients with CTCL is not known.

Methods, Results: We utilized the Surveillance, Epidemiology, and End Results (SEER) and TriNetX databases to perform a population level retrospective cohort analysis of patients with cutaneous lymphoma who developed a second primary malignancy. Risks of subsequent malignancy were evaluated by standard incidence ratios for SEER data and relative risk for TriNetX data.

Patients with pCBCL were at risk of developing thyroid and renal cancers (SIR, 2.27; 95% CI 1.32-3.63 and 1.54; 95% CI 1.04-2.20). When stratified by sex, males with pCBCL had an increased risk of melanoma (SIR 1.49; 95% CI1.03-2.09), bladder (SIR 1.42; 95% CI 1.01-1.94), and prostate cancers (SIR 1.29; 95% CI 1.07-1.54), and females had an increased risk of lung cancer (SIR 1.69; 95% CI 1.25-2.24). Patients with CTCL had increased risk of keratinocyte carcinomas compared with general population controls (RR 1.64; 95% CI 1.51-1.77), including increased risks of cutaneous squamous cell carcinoma (cSCC; RR 1.95; 95% CI 1.73-2.20) and basal cell carcinoma (BCC; RR 1.52; 95% CI 1.38-1.67). Across anatomic sites, the highest risks were cSCC on the trunk (RR 2.30; 95% CI 1.63-3.24) and BCC on the extremities (RR 1.72; 95% CI 1.41-2.10).

Conclusion: The risk of subsequent malignancies was increased in patients with cutaneous lymphomas. Given these findings, cutaneous lymphoma patients can benefit from routine skin cancer

screenings. Additionally, appropriate counseling and referral for further consultation if concerning symptoms are present can be advantageous to pCBCL patients.

Learning Objectives:

- Assess the risk of developing second primary malgnancies in patients with cutaneous lymphoma

1B.06 Real-World Outcomes of Primary Cutaneous CD4+ Small/Medium T-Cell Lymphoproliferative Disorder in a Uk Supra-Regional Cutaneous Lymphoma Centre

Sebastian, Neenu[1], Bashir, Abraham E.[1,2], Lam, Mun W.[1], Shah, Farida[1], Rajasekaran, Amirtha[1], Amel-Kashipaz, Rasoul[1], Scarisbrick, Julia J.[1,2]

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Introduction: Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (PCSM-TCLPD) is a low- grade lymphomatoid proliferation. Initially classified as a CTCL variant in the 2018 WHO-EORTC classification and often clonal, it has since been redefined as an indolent lymphoproliferative disorder. However, optimal post-diagnostic surveillance remains undefined and relapses may occur.

Methods, Results: Retrospective analysis of all patients diagnosed with PCSM-TCLPD at a UK supra-regional cutaneous lymphoma centre between September 2018 and November 2025. Forty patients were identified (male:female 1:1). The median age at diagnosis was 57.0 years (range:4–79). Lesions were most frequently located on the head and neck (55.0%). Morphologically, 80% were solitary papules or nodules, and 15% were plaques. Imaging (CT/PET-CT) was performed in 38/40 patients with no PCSM-TCLPD-related systemic disease detected. Euroclonality-NGS was conducted on 6 biopsies, identifying diagnostic clonal populations in 50%(n=3). All clonal cases demonstrated TRBD1 and TRBD2 gene rearrangements.

Treatment consisted of excision in 55% (n=22), radiotherapy in 25%, and combined excision and radiotherapy in 10%. Six patients (15%) experienced recurrence, with a median time to recurrence of 36 months (range 6–132). Five patients experienced a single recurrence, and one had three recurrences, (eight events total). These were managed with radiotherapy(n=6), spontaneous resolution(n=1), or treatment at another centre(n=1). One patient with recurrent disease developed stage IV peripheral T-cell lymphoma, 14 years after diagnosis.

Follow-up was variable, typically annual(n=22). Seven patients (17.1%) were discharged after a median of 5 years. There were no disease-related deaths. Secondary malignancies were identified in three patients (PTCL, breast cancer and pancreatic GIST).

Conclusion: PCSM-TCLPD is indolent, although late recurrences may occur. Systemic disease is rare despite frequent baseline imaging. Our observed recurrence rates and secondary malignancies support annual follow-up for five years, while routine CT or PET-CT imaging and prolonged surveillance may not be necessary for most patients.

Learning Objectives:

1. PCSM-TCLPD follows an indolent clinical course with rare systemic involvement, despite frequent use of baseline CT or PET-CT imaging at diagnosis.
2. Cutaneous recurrences occur in approximately 15% of patients, often several years after initial diagnosis, supporting the need for ongoing—but not prolonged—clinical follow-up.
3. Although prognosis is good, secondary malignancies can occur, warranting continued clinical vigilance.

1B.07 Clinical Outcomes in Primary Cutaneous Peripheral T-cell Lymphoma, Not Otherwise Specified

Stuver, Robert[1], Savage, Kerry[2], Lytle, Andrew[2], Epstein-Peterson, Zachary D.[1], Geller, Shamir[1], Ghione, Paola[1], Imber, Brandon[1], Lezcano, Cecilia[1], Moore, Zachary[1], Moskowitz, Alison[1], Moy, Andrea[1], Virgen, Cesar A.[1], Zain, Jasmine[1], Pullitzer, Melissa[1], Horwitz, Steven M.[1]

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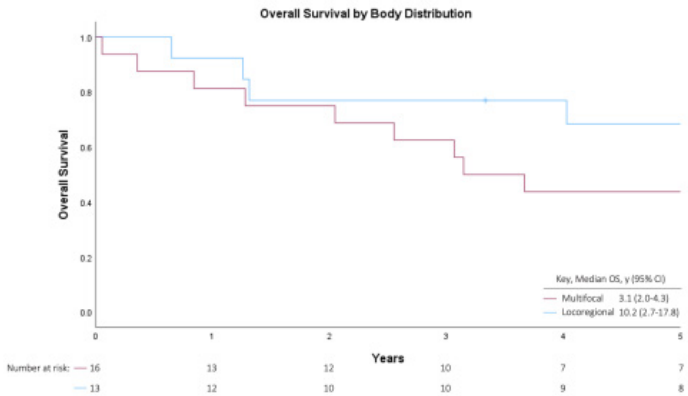
Introduction: Primary cutaneous peripheral T-cell lymphoma, not otherwise specified (PCPTCL-NOS) is an incompletely characterized T-cell lymphoma subtype. The clinical outcomes of this entity remain uncertain, making optimal clinical management challenging.

Methods, Results: PCPTCL-NOS was defined as pathologically-confirmed PTCL-NOS confined to the skin at diagnosis. All other T-cell lymphomas, including MF, CD4+ small/medium T-cell lymphoproliferative disorder (TLPD), and CD30+ TLPDs, were excluded. Except one case with unavailable tissue, all cases were reviewed by a cutaneous lymphoma dermatopathologist. When possible, additional immunohistochemical stains were performed for diagnostic clarity, in particular CD30, TCR-delta and EBER. Clinical data and photos (when available) were obtained from the medical record.

A total of 30 patients were identified. The median age was 59 years. As for lesion distribution, 16 patients had multifocal lesions across multiple body regions and 13 had localized presentations (one patient had missing data on distribution). Sixteen patients had lesions described as tumors. The predominant immunophenotype was CD4+/CD8– (80%). As for initial treatment, 16 patients received systemic therapy (predominantly CHOP-based), 11 received radiation, and three were observed for various reasons. Treatment differed by distribution, with systemic therapy favored for multifocal disease (75%) and radiation for localized (70%). For all patients, two-year progression-free (PFS) and overall survival (OS) was 35% (95% CI, 17-52) and 77% (62-92), respectively. Survival varied by distribution; two-year PFS/OS for localized versus multifocal was 46%/77% versus 20%/75% (median PFS/OS for localized versus multifocal was 1.5/10.2 years versus 0.6/3.1 years). Two-year PFS/OS for multifocal disease treated with CHOP-like therapy was 25%/63%, and two-year PFS/OS for localized disease treated with radiation was 22%/67%. Twenty patients died, ten from lymphoma.



Conclusion: PCPTCL-NOS is a rare T-cell lymphoma with uncertain clinical outcomes. In this cohort, patients with multifocal disease fared worse than those with localized presentations despite more frequent combination chemotherapy, suggesting that clinical distribution may have prognostic implications.

Learning Objectives:

- Primary cutaneous peripheral T-cell lymphoma, not otherwise specified (PCPTCL-NOS) is a distinct WHO entity with incompletely defined clinical behavior.
- Treatment approaches for PCPTCL-NOS vary by clinical distribution (multifocal versus localized), with systemic combination chemotherapy more common for multifocal disease and radiation more common for localized disease.
- Survival outcomes for multifocal disease are worse than for localized disease, despite more frequent use of combination chemotherapy.

SESSION 2: RISK, DISPARITIES, AND PROGNOSTIC DETERMINANTS IN CUTANEOUS T-CELL LYMPHOMA

2.01 Identifying High-Risk Early-Stage Mycosis Fungoides: Prognostic Insights from the PROCLIPI Cohort

Bashir, Abraham E.[1,2], Evision, Felicity[1], Kempf, Werner[3], Cerroni, Lorenzo[4], Willemze, Rein[5], Kim, Youn H.[6], Scarisbrick, Julia J.[1,2], On behalf of PROCLIPI colloborators

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Introduction: A prognostic index for advanced MF/SS has recently been published combining age at diagnosis > 60 years, large cell transformation in skin, raised serum LDH and nodal effacement. This CLIPI successfully stratifies advanced MF/SS patients into low, medium and high-risk with significantly different 5-year overall survival and progression free survival. A CLIPI for early MF is urgently needed with the median age of diagnosis at 57 years and the 5-year survival between 72.4%-95.4%.

Methods, Results: 'PROCLIPI'(ClinicalTrials.Gov ID:NCT02848274) is prospectively collecting pre-defined datasets including clinical, pathological, haematologic, radiologic, genotypic, treatment data and quality of life, in newly diagnosed MF/SS patients. 801 patients have been passed clinicopathological review by our Central Review Team. This includes stage IA (49.2%,n=394), stage IIA(42.6%,n=341) and stage IIA(8.2%,n=66). Median age at diagnosis was 57years(IQR:43-68yrs) with a male:female ratio of 1.7. In a median follow up of 59months 12.1% progressed to advanced disease, 10.4% have died including 4% from MF. In multivariate analysis factors associated with progression to advanced disease, and worse survival, included plaques(p<0.001), nodal enlargement(Nx-N2)(p<0.001), confluent erythema(p=0.002) and large cell transformation(LCT) in skin(p=0.002). Notably plaques have a high correlation with disease progression and poor overall survival (83.9% 5-year survival) compared to patients with patch only disease (94.8% 5-year survival).

Conclusion: PROCLIPI has found low 5-year survival rates in early-stage MF coupled with a median age of diagnosis of 57years there is a marked reduction in life expectancy. However, the 5-year survival rate for those with patch only disease is similar to a 57-year-old in Europe. PROCLIPI has identified important factors for worse outcome allowing these at-risk patients to be identified using markers such as plaques, nodal enlargement and LCT in skin. The data highlights the need for better stratification of early-stage patients to allow improved management.

Learning Objectives:

1. Identify clinical and pathological risk factors from the PROCLIPI study that predict progression and reduced survival in early-stage mycosis fungoides.
2. Apply PROCLIPI prognostic insights to stratify early-stage MF patients by risk and inform clinical management decisions.

2.02 Racial Differences in Prognosis in Mycosis Fungoides and Sézary Syndrome: Analysis from the BEACON (Building an Equitable and Collaborative Oncology Network)-CTCL Cohort

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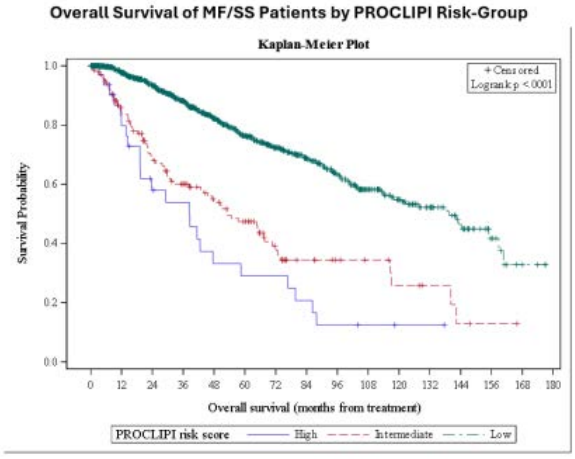
Introduction: Staging and prognostic assessment of Mycosis fungoides (MF) and Sézary syndrome (SS) are cumbersome and fail to adequately determine treatment choice or predict outcomes. Black patients have an increased burden of disease and unique clinical presentations, yet are underrepresented in existing prognostic models, such as PROCLIPI (Prospective Cutaneous Lymphoma International Prognostic Index). We sought to evaluate existing prognostic algorithms in a racially diverse US-based population.

Methods, Results: Adults with MF/SS diagnosed between 2010–2024 at nine U.S. academic centers in the BEACON-CTCL consortia were analyzed. Clinical, pathologic, and staging data were abstracted including PROCLIPI prognostic variables. Univariate and multivariable models were performed. Overall survival (OS) was evaluated using Kaplan-Meier analysis and multivariable Cox proportional hazards models.

1,523 patients including 901 (59%) White and 524 (34.4%) Black patients were eligible. 66% had early-stage and 34% had advanced-stage disease at diagnosis. Black patients were more likely to have elevated LDH, extracutaneous involvement, and advanced stage. In the initial analysis, 1,170 early- and advanced-stage patients were stratified by PROCLIPI risk group. PROCLIPI was prognostic for OS in Black and White patients across stages, however Black patients in the intermediate- and high-risk categories had shorter median OS compared with White patients. Analyzing by stage, adverse prognostic factors among patients with early-stage disease (1a-2a) included age >60 years, elevated LDH at diagnosis, T2 classification, and elevated nodal stage (N1, N2, Nx). In advanced-stage (2b-4b), elevated LDH and large cell transformation were the dominant prognostic factors.



PROCLIPI risk score	N	Event	Censored	Median Survival (95% CI)	12 Mo Survival	24 Mo Survival	60 Mo Survival
High	32	23 (72%)	9 (28%)	38.4 (19.1, 58.5)	79.8% (60.4%, 90.4%)	58.1% (37.9%, 73.7%)	29.0% (13.2%, 47.0%)
Intermediate	141	75 (53%)	66 (47%)	53.1 (38.2, 70.7)	84.4% (77.0%, 89.5%)	68.8% (59.9%, 76.1%)	47.4% (37.8%, 56.4%)
Low	991	222 (22%)	769 (78%)	139.5 (116.7, 158.8)	97.6% (96.4%, 98.4%)	93.3% (91.4%, 94.8%)	76.4% (72.8%, 79.6%)

Conclusion: We present the largest, most racially diverse MF/SS US cohort ever reported. While current models were predictive of survival across patient groups, stratification was heavily skewed toward low-risk, suggesting additional clinical variables relevant for diverse US populations should be studied. Prognostic models will be updated to include the larger cohort, additional clinical variables, and lymphoma-specific-survival at the time of the meeting.

Learning Objectives:

1. Review current staging and prognostic algorithms in CTCL
2. Identify shortcomings of current prognostic and staging models in diverse US populations.
3. Review performance of the PROCLIPI prognostic model in a diverse US population and discuss additional prognostic clinical variables.

2.03 Colour Lines in Cancer? Exploring Race as Determinant of Cutaneous T-Cell Lymphoma Outcomes, Using the Global PROCLIPI Cohort

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Introduction: Emerging evidence, primarily from single centres or geographical regions, suggests that race/ethnicity impacts CTCL incidence, treatment access, and disease outcomes. This research explores race as a determinant of CTCL outcomes and Health-related quality of life(hrQoL) measures on a global cohort from over 50 expert CTCL centres, registered with PROCLIPI(ClinicalTrials.Gov ID:NCT02848274).

Methods, Results: Analysis of PROCLIPI patients that had race/ethnicity self-reported(n=1707) from all PROCLIPI centres. Categorisation of ethnicity/race were matched and grouped across the global regions to allow for comparison.

Primary analysis compared variables between Caucasian(C) (75%,n=1287) and non-Caucasian(NC)(25%,n=425) patients found that both cohorts had male dominance (NC:59.5%,C:64.3%) and a similar stage distribution at diagnosis (early-stage: NC:79.8% vs C: 79.1%). However, NC had a significantly($p<0.001$) lower median age at diagnosis of 55 years(IQR:39,68 vs C:63years,IQR:39,68), despite experiencing a higher diagnostic delay (NC:48months,IQR:24,90 vs C:36months,IQR:12,84), presenting with significantly($p<0.0001$) higher mSWAT score (NC:20,IQR:9,48 vs C:15,IQR:6,43.58).

Progression to advanced stage disease occurred more frequently in Caucasians (76.7% vs NC:66.1%), and within a shorter median time to progression of 17months(IQR:7,37 vs NC:20months,IQR:6,37.25) than NC($p>0.05$). Caucasian patients also had a significantly higher overall mortality rate (16%) in comparison to non-Caucasian patients (10.1%) ($P=0.0002$), however using a cox regression model, with adjustment for age, there was no significant difference($p>0.05$) in overall survival between the two cohorts.

HrQoL data measured at diagnosis(n=505), by Skindex29, found that non-Caucasian patients had greater impairment in overall QoL (33.1,IQR:16.4,50.2 vs C:27.5,IQR:14.5,44.9) and experienced significantly worse psychological distress ($p=0.01$) (emotions domain score: NC:45,IQR:22.5,60 vs C:32.5,IQR:17.5,52.5).

Conclusion: In this large global CTCL cohort, race was associated with age at diagnosis, diagnostic delay, disease burden, and health-related quality of life. Despite higher mSWAT scores and poorer emotional wellbeing in non-Caucasian patients, survival outcomes were similar after age adjustment, highlighting inequities beyond mortality that warrant targeted global research efforts such as PROCLIPI.

Learning Objectives:

1. Describe racial/ethnic differences in clinical presentation, diagnostic delay, disease burden, and progression in CTCL using global PROCLIPI data.
2. Interpret disparities in health-related quality of life and psychological distress by race/ethnicity and their implications for equitable CTCL care.

2.04 Racial and Ethnic Disparities in T-Cell Receptor Beta Repertoire in Cutaneous T-Cell Lymphoma

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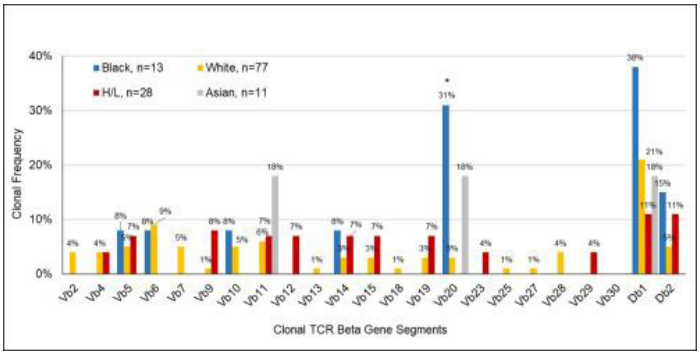
Introduction: Mycosis fungoides (MF) and Sézary syndrome (SS), the most common subtypes of cutaneous T-cell lymphoma (CTCL), are characterized by clonal proliferation of skin homing memory T-cell and exhibit well-documented disparities in clinical outcomes across racial/ethnic groups. Sequencing of T-cell receptor (TCR) has guided the diagnosis and advanced understanding of disease progression by enabling precise identification, quantification and tracking of TCR clones. However, race/ethnicity stratified analysis of TCR clonotypes remains largely unexplored in CTCL. Our aim is to evaluate the detection rate of clonal TCRβ gene segments and compare their frequency among ethnic groups in patients with CTCL.

Methods, Results: This single-center retrospective cohort study includes patients diagnosed with MF and SS who underwent next generation sequencing of lesional skin to assess TCRβ CDR3 clonality.

DNA was extracted from formalin-fixed paraffin-embedded skin biopsies. Clonal frequency was compared between the ethnic groups by the Freeman-Halton extension of the Fisher's exact test. Multiple comparison adjustment was based on Bonferroni method with p<0.00179 (0.05/28) being considered statistically significant.

We identified 129 MF/SS patients with skin biopsies collected from June 2020 to November 2024. Vb20 and Db1 were more frequently detected in Blacks compared to other racial groups. All patients with Vb20 had advanced disease and aggressive histological subtypes, but the frequency of clonal Vb20 was statistically significantly different between the ethnic/race groups (Black: 4/13=31%, White: 2/77=3%, Asian: 2/11=18%, Hispanic: 0/28=0%; p=0.0012). None of the other TCRβ genes were statistically significantly different between these groups.



Conclusion: TCR sequencing is an important test that should be included in the diagnosis algorithm of CTCL patients. Early identification of patients at risk may help quide selection of patients who could benefit from targeted therapies. Treatment strategies targeting Vb20, microbial dysbiosis, and boosting immune system via PD1/PD-L1 pathway may represent an opportunity to improve outcomes in Black patients.

Learning Objectives:

- Identify the differences between TCRβ clonotypes among race and ethnic groups in CTCL.
- Discuss the early selection of patients who may benefit from targeted therapies.

2.05 Bridging Racial Disparities in Mycosis Fungoides Diagnosis Through Dermoscopy

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Introduction: Mycosis fungoides (MF) often mimics benign inflammatory dermatoses, resulting in frequent misdiagnosis and diagnostic delay. Dermoscopy is a useful noninvasive adjunct in MF diagnosis; however, the existing literature is largely derived from White patients, limiting generalizability to other racial groups.

Methods, Results: We conducted a retrospective study of 146 patients whose skin lesions were dermoscopically imaged and photographed before biopsy at our cutaneous lymphoma clinic between 2000-2020. 47 patients were self-reported African American (AA)/Black and 99 non-AA/Black. Dermoscopy photographs of 157 clinicopathologically confirmed MF lesions and 58 inflammatory dermatoses lesions were independently evaluated for dermoscopic features by two blinded raters using a standardized survey. Dermoscopic features were compared by race and diagnosis, including only lesions for which both raters were in complete agreement.

Among MF lesions, AA/Black patients demonstrated a higher prevalence of background reticular network (92.2% vs 12.6% in non-Black patients; p<0.001) and absence of visible blood vessels (40% vs 5.2%; p<0.001). MF lesions in Non-AA/Black patients more frequently exhibited dotted vessels (63.5% vs 29.2% in AA/Black patients; p<0.001) and focal yellow crusts (26.2% vs 8.8%; p=0.006). Scale-related features did not differ significantly by race. Similar racial differences in dermoscopic patterns were observed in inflammatory lesions. No significant dermoscopic differences were observed between MF and inflammatory lesions, nor between early-stage MF patches or plaques and psoriasiform or eczematous lesions, either overall or within each of the two racial groups studied. Interrater agreement was high for scale and reticular network but low for vascular morphology.

Conclusion: Dermoscopic features of MF vary across racial groups. Awareness of these variations may enhance diagnostic accuracy and help reduce delays and racial disparities in MF diagnosis.

Learning Objectives:

1. Describe dermoscopic features of mycosis fungoides lesions in Black versus non-Black patients.
2. Recognize limitations of dermoscopy in distinguishing mycosis fungoides from inflammatory mimickers.

2.06 Mycosis Fungoides in the Pediatric Population in Chile: a Retrospective Study

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1. Pontificia Universidad Católica de Chile, Santiago, Chile, 2. Clinica Alemana de Santiago, Santiago, Chile

Introduction: Pediatric mycosis fungoides (MF) is an uncommon variant of cutaneous T-cell lymphoma with distinct clinical and histopathological features. Data from Latin American populations are limited. This study aimed to characterize the clinical presentation, histological features, and outcomes of pediatric MF in Chile between 2000 and 2022.

Methods, Results: A retrospective cross-sectional study was conducted including patients under 18 years diagnosed with MF at a referral center in Chile between 2000 and 2022 (n=19). The mean age at diagnosis was 10 years (range 4–17), with male predominance (63%). The median diagnostic delay was 24 months (range 1–72).

Hypopigmented MF was the most frequent subtype (89%), presenting mainly as macules (74%) and plaques (42%) involving the trunk and extremities. No tumors or erythroderma were observed. Immunohistochemistry showed CD8+ predominance in 72% and epidermotropism in 95% of cases.

At diagnosis, 42% were stage IA and 58% stage IB. Narrowband UVB was the main treatment (89%). Clinical outcomes included complete remission in 42% and relapsing disease in 42%, with no disease-related mortality.

Despite a mean follow-up of 5 years, 63% of patients had not attended follow-up visits in the last two years.

Conclusion: Pediatric MF in this cohort was predominantly hypopigmented with a CD8+ phenotype and favorable prognosis, consistent with previous reports. However, significant diagnostic delay and high loss to follow-up represent major challenges. These findings highlight the need for increased awareness and structured long-term follow-up strategies in pediatric populations.

Learning Objectives:

1. Recognize the predominant clinical and histopathological features of pediatric mycosis fungoides (MF) in Chile.
2. Identify the common diagnostic delays and follow-up challenges in pediatric MF.

2.07 Area Deprivation and Disease Severity in Adult Patients with Cutaneous T-Cell Lymphoma

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Introduction: Cutaneous T-Cell Lymphomas (CTCL) encompass a heterogeneous group of rare malignancies with variable clinical manifestations and disease severity. While disease stage at presentation is a key prognostic factor, the relationship between socioeconomic status and outcomes in CTCL remains poorly understood. The Area Deprivation Index (ADI) is a tool that evaluates neighborhood-level socioeconomic disadvantage through a variety of different factors, such as income, education, employment, housing quality, and environmental factors including pollution. Given this, ADI is a resource that can be used to capture the socioeconomic conditions of an area, while providing a deeper understanding of the various factors that adversely affect health outcomes. Our objective is to determine the association between socioeconomic deprivation, as measured by the ADI, and staging at the time of presentation to an academic center. The incidence of post-diagnosis complications including sepsis, bacteremia, large cell transformation, superinfection, and/or death in adult patients with CTCL will also be assessed.

Methods, Results: We performed a retrospective cross-sectional chart review of patients with CTCL evaluated at the University of Wisconsin between January 1st, 2015, and December 31st, 2025. Patients with documented CTCL diagnoses prior to 2015 or absent staging data within one year of diagnosis were excluded from the study. Variables extracted include CTCL subtype, stage, immunosuppressive status, and ADI at the time of diagnosis. Data abstraction is ongoing, and approximately 150 patients will meet the eligibility criteria. Descriptive analyses and statistical comparisons will be performed.

Conclusion: This study will help to elucidate patient populations at risk for poor prognosis of CTCL. Additionally, it will provide further evidence to support access to specialty care for medically underserved patients.

Learning Objectives:

- Recognize how neighborhood-level socioeconomic disadvantage may influence access to dermatologic care for patients with Cutaneous T-Cell Lymphoma.
- Examine potential correlations between neighborhood-level socioeconomic disadvantage and complications associated with Cutaneous T-Cell Lymphoma.

SESSION 3A: T CELLS GONE ROGUE: SINGLE-CELL, SPATIAL, AND MOLECULAR FRONTIERS IN CTCL

3A.01 Single-cell Proteomic and Transcriptomic Profiling of Lesion-Specific Aberrant T Cell States and Checkpoint-Dominated Microenvironment of Mycosis Fungoides

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Introduction: Mycosis fungoides (MF) is a primary cutaneous T cell lymphoma, marked by the differentiation of aberrant $CD4^+$ T cells in a progressively remodelled tumor microenvironment (TME). Although negative immune checkpoints are implicated in advanced MF, the lesion-related differentiation of aberrant T cell states and their interactions with immunosuppressive immune and stromal compartments remain incompletely understood.

Methods, Results: Single-cell mass cytometry was performed on thirty lesions (patch, plaque and tumor) from MF patients' skin biopsies and integrated comparative analysis with nine publicly available scRNA-seq datasets from MF patients. Aberrant T cell phenotypes, immune subsets and checkpoint expression were examined across all MF lesions and related to clinical parameters.

Mass cytometry showed a progressive accumulation of aberrant $CD4^+CD7^-CD26^-$ T cells, accompanied by increasing CCR4 and PD-1 expression, peaking in tumor lesions. Tumors exhibited also selective enrichment of PD-1^+ $CD4^+$ and $CD8^+$ T cells, together with immunosuppressive PD-$L1^+$ populations, including regulatory T cells, M2 macrophages, and memory B cells. Higher levels of PD-$L1^+$ memory B cells were associated with reduced progression-free survival (PFS).

scRNA-seq identified three dominant aberrant $CD4^+$ T cell states forming a continuous evolutionary trajectory: a TOX^{lo} effector-memory-like state in patches, a TOX^+ Th2/central-memory-TRM-like state in plaques and a tumor-restrictive TOX^{hi} stress-adapted state embedded within cancer-associated fibroblast niches. Tumor lesions showed pronounced stromal reprogramming with CAF expansion and replacement of conventional dendritic cells (DCs) with PD-$L1^+$ $LAMP3^+$ activated DCs.

Conclusion: Mass cytometry and scRNA-seq analyses revealed a lesion-specific cellular map of MF severity, linking to clinical progression and supporting stage-adapted therapeutic strategies spanning from immune-sparing approaches in early patches to PD-1/PD-L1 and CCR4 blockade in plaques and tumours, potentially enhanced by immunometabolic modulation of the TME, including B cell depletion and macrophage reprogramming.

Learning Objectives:

1. Describe lesion-specific immune and aberrant T cell population in mycosis fungoides across patch, plaque, and tumor lesions using single-cell mass cytometry and scRNA-seq.
2. Understand the association of PD-1/PD-L1 expression with disease severity, including regulatory immune populations and cancer-associated fibroblast niches.

3A.02 Deep-learning Based T-Cell Recognition and Automated Clone Estimation in Early-stage Mycosis Fungoides: a Proof of Concept Study (TRACE-MF)

Valkema, Pieter A.[1], Brussee, Siemen[1], Doeleman, Thom[1,2], van der Perk, Kaley R.[1], de Oude, Alyssa[1], Singh, Amrita Kim[1], Baelde, Hans J.[1], Kers, Jesper[1,3], Vermeer, Maarten H.[1], Schrader, Anne M.R.[1]

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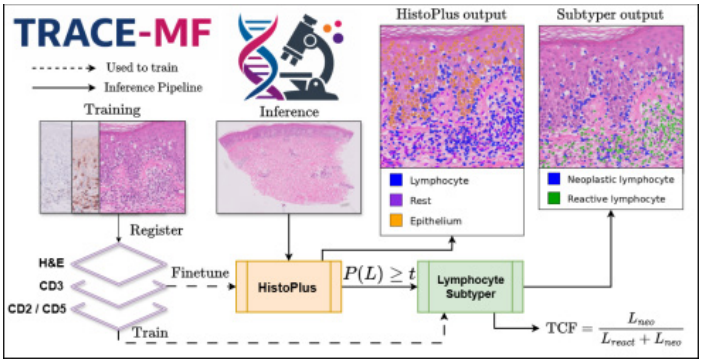
Introduction: In early-stage mycosis fungoides (eMF), neoplastic lymphocytes are difficult to distinguish from reactive lymphocytes because of morphological overlap. We aimed to develop deep-learning (DL) algorithms for automated detection and quantification of neoplastic T cells in eMF skin biopsies.

Methods, Results: We constructed a nucleus-level annotated eMF whole-slide image (WSI) dataset, linking immunophenotype to H&E morphology using multiplex immunohistochemistry (mIHC). Biopsies from eMF patients, selected for CD2 and/or CD5 loss, underwent sequential destain–restain mIHC combining H&E with CD3 and CD2 or CD5. Nuclei were segmented and manually labelled via co-registration of the slides. The HistoPlus model was fine-tuned to classify nuclei as lymphocyte, epithelial, or other using Leave-One-Slide-Out (LOSO) cross-validation. Lymphocyte detection on each left-out slide used a precision-constrained threshold (P≥0.90). A CNN subtyping model was then trained (LOSO) to distinguish neoplastic (marker-loss) from reactive (no marker-loss) lymphocytes, and model-derived tumor clone fractions (TCFs) were compared with annotation-based ground truth.

The dataset comprised 14 eMF WSIs with a total of 165,998 labeled nuclei: 54,827 lymphocytes (20,179 neoplastic; 34,648 reactive), 32,977 epithelial cells, and 78,194 other cells. Lymphocyte detection achieved PR-AUC 0.78±0.23 across LOSO folds (F1 0.68±0.20; precision 0.66±0.26; recall 0.76±0.21). Under the precision constraint, the median threshold was 0.72, yielding median recall ≈0.25. The subtyping model differentiated neoplastic from reactive lymphocytes with AUC–ROC 0.742±0.06. Feature analysis revealed reactive lymphocytes formed dense neighborhoods, whereas neoplastic lymphocytes were more isolated, exhibited higher same-type assortativity and epithelial proximity, had larger nearest-neighbor distances, larger and elongated nuclei, and more homogeneous chromatin texture (Mann–Whitney U with FDR-BH correction, adjusted p<0.05). Model-derived TCFs correlated moderately with annotation-based tumor burden (r=0.3642, MAE=0.171±0.091).



Conclusion: Deep-learning models trained on mIHC-derived cell-type annotations can detect and subtype lymphocytes in eMF using routine H&E slides. Modeling nuclear and spatial features enables automated quantification of TCF in MF.

Learning Objectives:

1. Understand how multiplex immunohistochemistry can be used to generate nucleus-level cell-type annotations as ground truth for training deep learning (DL) models in early-stage mycosis fungoides (eMF).
2. Assess whether DL can distinguish between neoplastic and reactive lymphocytes in H&E whole slide images of eMF, enabling automated quantification of tumor clone fractions (TCFs).
3. Identify key nuclear and spatial features that distinguish neoplastic from reactive T cells.

3A.03 Single-cell Profiling of Advanced-Stage Mycosis Fungoides Reveals Distinct Immune and Stromal Responses in Tumor Versus Erythrodermic Lesions

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Introduction: Advanced-stage cutaneous T-cell lymphomas (CTCL) manifest clinically as either skin tumor formation or erythroderma, previously attributed to tissue-resident versus central memory malignant T-cell phenotypes, respectively. However, the specific pathophysiological mechanisms underlying lesion formation, particularly those facilitating vertical tumor growth, remain insufficiently characterized.

Methods, Results: To address this gap, we compared molecular profiles of erythrodermic CTCL (erythrodermic MF and Sézary Syndrome) with tumor-stage MF lesions using single-cell RNA sequencing combined with T-cell receptor sequencing. As expected, all samples harbored a single strongly expanded malignant *CD4+TOX+* T-cell clone, with decreased tissue residency markers such as *CXCR4* and *CD69* in erythroderma, consistent with their highly migratory behavior. Tumor lesions demonstrated an overall Th2/Tc2 bias characteristic of advanced-stage disease, reflected by high expression levels of macrophage-derived *CCL17, CCL13,* and *AREG*. In contrast, this type 2 bias was much less pronounced in erythroderma, which retained significant expression of type 1-associated markers such as *CXCL9,* challenging the general Th1/Th2 dichotomy in early

versus advanced-stage CTCL. Consistent with previous reports, tumor lesions displayed considerable inter-patient cellular and molecular heterogeneity, whereas erythroderma exhibited a more uniform transcriptional profile, despite encompassing both Sézary Syndrome and erythrodermic MF. Tumors consistently showed enhanced expression of *CCL19* in proinflammatory fibroblasts and harbored increased frequencies of *IL32+CD69+IFI44L-* activated B-cells, potentially contributing to the formation of a tumor-permissive tertiary lymphoid structure. Additionally, tumor lesions demonstrated upregulation of markers associated with vascular remodeling, angiogenesis, and extracellular matrix deposition by endothelial cells. By contrast, erythroderma exhibited a higher degree of epidermal activation and markers of anti-angiogenesis, such as *CXCL14* within stromal cells, which may actively counteract vertical tumor growth in these patients.

Conclusion: Taken together, these findings provide novel insights into the pathogenesis of advanced-stage CTCL and highlight molecular features that may serve as potential therapeutic targets.

Learning Objectives:

1. To compare the molecular features underlying tumor-stage and erythrodermic manifestations of advanced-stage CTCL

3A.04 Integrated Transcriptomic and Microbiomic Profiling of Keratinocytes in Erythrodermic Cutaneous T-cell Lymphoma Identifies Distinct Epidermal-microbial Patterns

De Jong, Katherine[1], Ostroff, Eleanor[1], Stagaman, Elise[2], Pang, Yanzhen[1], Ren, Ziyou[1], Siddiqui, Umar[2], Guitart, Joan[1], Burns, Michael[2], Zhou, Xiaolong[1]

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Introduction: Epidermal-microbial interactions in erythrodermic skin disease remain poorly understood, including for malignant erythroderma. We performed integrated microbial and epidermis-focused spatial transcriptomic profiling to define microbe gene expression relationships in CTCL erythroderma compared with benign erythrodermas, such as atopic dermatitis (AD), psoriasis (PSO), drug reactions (DR), and autoimmune disease (AID).

Methods, Results: Seventeen erythrodermic patients (CTCL, AD, PSO, DR, AID) and four healthy controls (HC) were studied. Skin swabs underwent full-length 16S rRNA sequencing to define microbial composition, and epidermis from lesional biopsies was analyzed using NanoString GeoMx DSP.

Erythrodermic CTCL skin showed increased Staphylococcus (S.) lugdunensis and decreased S. hominis relative abundance compared with HC. S. aureus trended toward significance ($p = 0.06$). In all erythroderma subtypes, S. hominis-dominant, higher-diversity states were linked to epidermal differentiation and immune regulation (WNT8A, IGF1R, HLA-C). S. aureus-dominant, low-diversity states were associated with keratinocyte stress and injury programs (KRT5, KRT14), NF-κB/IL-17 signaling (RELA, TRAF3IP2), and alarmin expression (TSLP) (adjusted $p<0.05$). Spatial transcriptomics further revealed thirty-three uniquely differentially expressed genes upregulated in CTCL keratinocytes related to three distinct keratinocyte programs: hyperproliferative stress response (KRT6A, KRT16, KRT14, SERPINB3); innate and adaptive immune activation (S100A7, S100A9, IRGM, CXCR4); and adaptations favorable for chronic metabolic stress (ENO1, PFKFB3, CALR, WIPI1,FTH1, BCL2L2) ($p<0.05$). This profile was unique to CTCL erythroderma in our dataset and aligns with prior research showing that malignant T-cells can alter keratinocyte biology and cause skin barrier disruption, contributing to microbial dysbiosis.

Conclusion: These findings show that integrating epidermal spatial transcriptomics with microbiome profiling elucidates microbe-keratinocyte interactions in CTCL and supports biologically informed diagnostic stratification of erythroderma.

Learning Objectives:

1. Participants should be able to recognize keratinocyte transcriptional programs in erythrodermic skin that differentiate malignant erythroderma from other benign subtypes.
2. Participants should be able to recognize basic associations between Staphylococcus aureus abundance and keratinocyte gene expression patterns in erythrodermic skin.

3A.05 The Role of CD84 (SLAMF5) in the Immunosuppressive Tumor Microenvironment of CTCL

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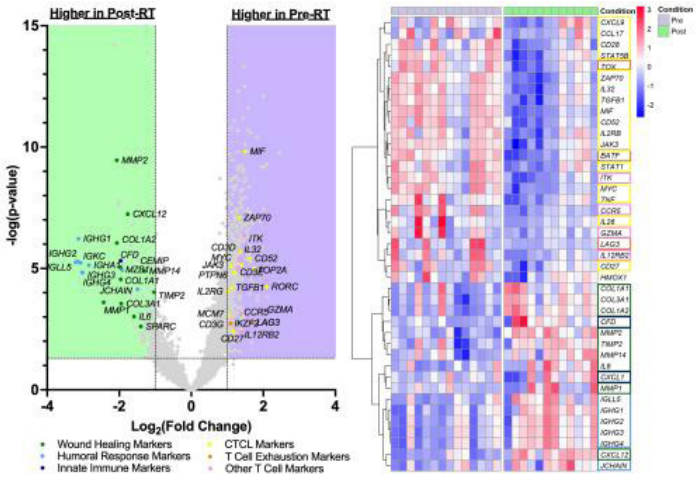
Introduction: Cutaneous T cell lymphomas (CTCL) are rare lymphoproliferative malignancies characterized by profound immune dysregulation and remodeling of the tumor microenvironment. CD84 (SLAMF5) is a signaling receptor expressed across multiple immune cells regulating cell communication, yet its function in CTCL remains to be explored. Defining CD84's role in tumor-immune interactions may reveal its potential as an immunomodulatory target.

Methods, Results: CD84 expression in CTCL lesions and healthy skin from our clinical dataset (GSE113113, n=48) was assessed by RNA sequencing and immunohistochemistry, followed by Qiagen Ingenuity Pathway Analysis (IPA) and OmicSoft gene correlation. CD84 mRNA and protein levels were examined in CTCL cell lines and monocytes using RT-PCR and Western blot. Flow cytometry was performed to characterize tumor-associated macrophage (TAM) polarization (CD163, CD206) and quantify intracellular chemokine production. It was further used to investigate immune checkpoint (PD-1/PD-L1) co-expression in the presence and absence of CD84-knockdown. Immunohistochemistry and migration assays were conducted using CD84-knockdown to evaluate CD84-dependent functional changes.

CD84 gene and protein expression were significantly upregulated in CTCL across disease stages compared to healthy controls. We identified CD84-associated pathways relevant to CTCL pathogenesis. Gene expressions of IL-15 ($r=0.525$, $p=0.0001$), IL-6 ($r=0.308$, $p=0.0001$), PLCG1 ($r=0.604$, $p=5.49e-06$), MTOR ($r=0.34$, $p=0.018$) and RARA ($r=0.419$, $p=0.003$) positively correlated with CD84 expression. While CTCL cell lines and monocytes expressed CD84 mRNA in different capacities, Western blot and flow cytometry confirmed corresponding CD84 protein expression. CTCL supernatant induced an M2-like macrophage phenotype with upregulation of CD84 mRNA and immunosuppressive cytokine IL10 mRNA. CD84-knockdown in M2-like TAMs reduced checkpoint co-expression, decreased TAMs migration and increased pro-inflammatory chemokines toward a pro-inflammatory M1-like state.



Conclusion: CD84 is upregulated in CTCL and drives M2-like TAM phenotypes. CD84-knockdown reduces checkpoints, impairs M2-like macrophage migration, and induces a CD84-dependent shift toward a pro-inflammatory M1-like state to support an anti-tumor immune response, highlighting its potential as therapeutic target.

Learning Objectives:

- Describe CD84 expression in CTCL and its association with a tumor-supportive microenvironment.
- Summarize the functional effects of CD84 inhibition on PD-1/PD-L1 expression and cell migration in CTCL.
- Discuss the potential of CD84 as an immunomodulatory therapeutic target in CTCL.

3A.06 Lesion-Specific Immune and Clonal Reprogramming Drives Chlormethine Gel Response and Treatment-Associated Dermatitis in Mycosis Fungoides

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Introduction: Chlormethine (CL) gel represents a first-line treatment option for early-stage mycosis fungoides (MF) patients, yet the immunologic and clonal effects underlying therapeutic response and treatment-induced dermatitis remain incompletely defined.

Methods, Results: Twelve early-stage MF patients treated with CL gel and two controls receiving topical corticosteroids or no treatment were prospectively followed for up to 18 months. Serial lesional biopsies were obtained at baseline, at best clinical response, and/or at the onset of treatment-associated dermatitis. High-dimensional mass cytometry (CyTOF, 48-marker panel) characterized aberrant T cell populations and immune subsets within the tumor microenvironment (TME). TCRβ clonality was assessed by high-throughput T cell receptor sequencing (HTS-TCR) to define clonal dynamics and distinguish aberrant from reactive T cell infiltrates. Bulk RNA sequencing of paired lesional samples was performed to characterize the transcriptional profiles associated with treatment response.

Clinical responses improved progressively, with partial responses (PR) emerging within the first month and most complete responses (CRs) after approximately one year. Eight patients developed dermatitis (mean onset 2.4 months). CL therapy induced consistent reductions of M2 macrophages and regulatory T cells (Tregs), with greater immune remodeling in patch compared to plaque lesions. Dermatitis was associated with early expansion of NK and Terminal Effector (TE) $CD8^+$ T cells and depletion of Th2, Treg, and ILCreg subsets. Lower baseline Treg frequencies and higher $CD8^+$/Treg ratios were significantly associated with CR. HTS-TCR demonstrated selective contraction of dominant aberrant clonotypes in responders, whereas control patients maintained stable high-frequency clones. Bulk RNA sequencing demonstrated coordinated transcriptional reprogramming in responders, including suppression of interferon, JAK/STAT, TNF-α, MYC, and inflammatory pathways, normalization of keratinocyte programs, activation of barrier-repair and metabolic pathways, and modulation of Wnt signaling.

Conclusion: In early-stage MF, CL gel triggers long-term effects of cytotoxic, immune, clonal, and transcriptional remodeling, which correlates treatment efficacy and treatment-related dermatitis.

Learning Objectives:

- Understand the immune and clonal dynamics induced by Chlormethine Gel in early-stage Mycosis Fungoides, including lesion-specific remodeling of T cell populations.
- Identify cellular and molecular markers associated with clinical response and treatment-related dermatitis, including Treg depletion, NK/$CD8^+$ expansion, and transcriptional reprogramming.

3A.07 Molecular Analysis of Irradiated Cutaneous T-Cell Lymphoma Tumors Suggests Markers Associated with Response and Risk of Recurrence

Ostroff, Eleanor[1], Holm, JoJo[1], Clarke, Lauren P.[1], De Jong, Katherine[1], Pang, Yanzhen[1], Hooper, Madeline J.[1], Evans, Spencer[1], Lu, Kurt Q.[1], Rangel, Stephanie M.[1], Mittal, Bharat[2], Guitart, Joan[1], Weichselbaum, Ralph R.[3], Ren, Ziyou[1], Zhou, Xiaolong A.[1]

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Introduction: Radiotherapy (RT) is a frequent treatment for cutaneous T-cell lymphoma (CTCL); however, little is known about the impact of RT on the tumor microenvironment. Moreover, factors influencing RT durability remain poorly defined. We performed parallel spatial whole-transcriptome profiling and proteomic profiling on CD4+ CTCL lesions before and after RT.

Methods, Results: Tape strips and punch biopsies of skin tumors pre- and post-RT from eight CTCL patients were obtained for spatial whole-transcriptomic (Nanostring GeoMx DSP) and proteomic

(Olink Inflammation 384 multiplex immunoassay) analyses. Spatial transcriptomic profiling of dermal tumor aggregates analyzed CD3+(CD8-), CD3+CD8+, and CD68+ cells (denoting malignant T-cells, cytotoxic T-cells, and macrophages). Proteomic results were compared with 27 healthy controls and 42 non-RT CTCL patients.

The pre-RT microenvironment was characterized by canonical CTCL markers (*IL32*, *TOX*, *STAT1/3/5B*, *JAK3*, *CD52*, *IL2RG*, *CD3D/E/G* [CD3+(CD8-) cells]; *TGFB1* [CD3+(CD8-), CD68+ cells]; proteins IL-32, CD4, CXCL9, MAPK9, and CCL17). T-cell exhaustion markers were upregulated *(LAG3*, *IKZF2*, *TOX*, *BATF* [all cell types]). Post-RT tumors exhibited upregulated wound healing/matrix remodeling markers (*MMP2*, *COL3A1*, *COL1A1*, and *TIMP2* [all cell types]; CDSN, MMP10, TIMP3, and VEGFA), innate immune activation (*CXCL12*, *CFD* [all cell types]; *CXCL1* [CD3+(CD8-) cells]; MICA/B), M1 polarization (*SLC11A1*, *IL18RAP* [CD68+ cells]; IL-18, IL-1B, HLA-DRA), and humoral response activation (*IGHG1/2/3/4*, *IGKC*, *IGLL5* [all cell types]; *IL6*, *JCHAIN* [CD3+(CD8-) cells]; TNFRSF13C, JCHAIN).

We identified upregulation of *SOD2* (log-fold-change 1.53) – a gene associated with radiation resistance – in patients whose tumors recurred. Additionally, we noted increased CTCL-associated inflammatory markers (*CXCL13*, 1.70; *CCL19*, 2.08; *YKL-40/CHI3L1*, 1.79; *S100A9*, 1.49; *IL-13*, 0.88; *VEGFD*, 2.06). Conversely, tumors in remission showed elevated humoral activation (*IGHG2*, 1.69; *IGHG3*, 1.76; *IGHG4*, 1.57; *IGLL5*, 2.58) and interferon signaling (*IFI44L*, 1.41), suggesting potential RT-induced anti-tumor immunity.

Conclusion: These findings suggest that combining RT with therapies that enhance interferons or target recurrence-related genes may amplify systemic anti-tumor effects, improving RT durability.

Learning Objectives:

1. Participants should be able to characterize the pre- and post-radiotherapy tumor microenvironment in CTCL.
2. Participants should be able to recognize certain genes associated with tumor recurrence post-radiotherapy.

SESSION 3B: OPTIMIZING MOGAMULIZUMAB THERAPY IN CUTANEOUS T-CELL LYMPHOMAS: REAL-WORLD EVIDENCE, SAFETY, AND LONG TERM OUTCOMES

3B.01 Real-world Use of Mogamulizumab: Final Analysis of the "FIL-MOGA" Study by the Italian Lymphoma Foundation (FIL)

Roccuzzo, Gabriele[1], Fava, Paolo[1], Rupoli, Serena[2], Morsia, Erika[2], Teoli, Miriam[3], Zinzani, Pier Luigi[4], Pileri, Alessandro[5], Tucci, Alessandra[6], Alberti Violetti, Silvia[7], Massone, Cesare[8], Ibatici, Adalberto[9], Bernardelli, Andrea[10], Nassi, Luca[11], De Lorenzo, Sonya[12], Bernuzzi, Patrizia[13], Pimpinelli, Nicola[14], Paulli, Marco[15], Onida, Francesco[16], Cantonetti, Maria[17], Loseto, Giacomo[18], Filotico, Raffaele[19], Simula, Maria Pina[20], Figuera, Amalia[21], Alaibac, Mauro S.[22], Cavalloni, Chiara[23], Fabbri, Alberto[24], La Porta, Agostino[25], Priolo, Giorgio[25], Marcheselli, Luigi[25], Quaglino, Pietro[1]

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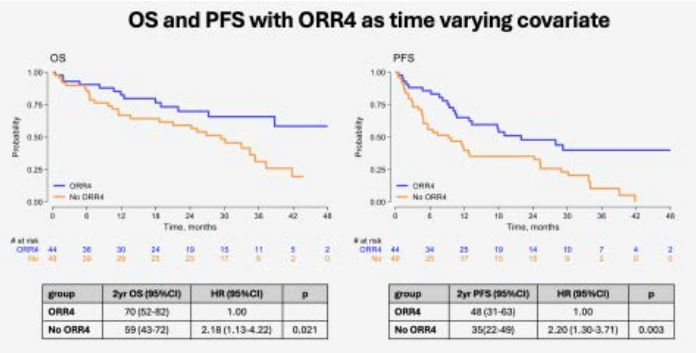
Introduction: In Italy, mogamulizumab became reimbursable at the end of 2020 for mycosis fungoides (MF) and Sézary syndrome (SS) after ≥1 prior systemic therapy. We report the first and largest Italian real-world study evaluating national prescribing patterns, effectiveness, and safety, and testing whether a durable global response (≥4 months) predicts long-term outcomes.

Methods, Results: This multicenter observational study enrolled patients from 18 Italian centers (01/2021–12/2023; data cut 11/2025). The primary endpoint was the proportion achieving a global objective response lasting ≥4 months (ORR4) and its association with overall survival (OS), progression-free survival (PFS), and time to next systemic treatment (TTNT). Of 100 enrolled, 98 were eligible (median age 63 years; 53% female; 71% had ≥2 prior systemic therapies). Median baseline mSWAT was 77 (range 3–152); 57% had elevated LDH; stages were IB 10%, IIA 6%, IIB 10%, III 22%, IVA1 26%, IVA2 17%, IVB 5%. In patients on treatment, the median number of cycles was 33 (range 17–60). At a median follow-up of 35 months, global ORR4 was 47% (95% CI 37–58); 11% had shorter responses and 48% had no response. Stage IV disease was associated with higher odds of ORR4 *versus* early-stage-disease (OR 3.94; 95%CI 1.40–11.1). Compartment-specific ORR was 50% in skin and 64% in patients with B2 blood involvement. Skin-related adverse events occurred in 33% and infections in 29% (grade I–III). Thirteen patients proceeded to HSCT, with 11 complete responses. Failure to achieve ORR4 was associated with higher risk of death (HR 2.92; 95%CI 1.50–5.57), progression (HR 3.25; 95%CI 1.91–5.54), and earlier next systemic therapy (HR 3.53; 95%CI 1.72–7.26).



group	2yr OS (95%CI)	HR (95%CI)	p
ORR4	70 (52-82)	1.00	
No ORR4	59 (43-72)	2.18 (1.13-4.22)	0.021

group	2yr PFS (95%CI)	HR (95%CI)	p
ORR4	48 (31-63)	1.00	
No ORR4	35(22-49)	2.20 (1.30-3.71)	0.003

Conclusion: Mogamulizumab shows meaningful and durable clinical benefit in Italian routine practice, with a manageable safety profile and a favorable role as a bridge to HSCT. ORR4 emerges as a solid surrogate endpoint strongly associated with OS, PFS, and TTNT.

Learning Objectives:

- ORR lasting ≥4 months (ORR4) was achieved in 47% and strongly predicted OS, PFS, and TTNT (non-ORR4: HR death 2.92; HR progression 3.25; HR next treatment 3.53).
- Mogamulizumab showed meaningful compartment activity (skin ORR 50%), with higher responses in patients with B2 blood involvement (ORR 64%).
- Mogamulizumab supported HSCT bridging in routine practice, with 11/13 transplanted patients achieving complete response.

3B.02 Patients with Mogamulizumab-Associated Rash Can Be Safely Retreated with Mogamulizumab with Durable Remissions: a Single Center Experience

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Washington University School of Medicine, St. Louis, MO, USA

Introduction: Mogamulizumab, a humanized monoclonal antibody targeting CCR4, is approved for relapsed/refractory mycosis fungoides (MF) and Sézary syndrome (SS). Although generally well tolerated, mogamulizumab-associated rash (MAR) is common and may lead to treatment discontinuation. Given limited therapeutic options in MF/SS, retreatment strategies are clinically relevant but understudied. We describe outcomes of mogamulizumab retreatment after MAR at our institution.

Methods, Results: We performed a single-center retrospective analysis from 2013-2025 of patients with MF/SS treated with mogamulizumab who had retreatment with mogamulizumab. Retreatment was defined as reinitiation after a >90-day treatment-free interval. Patient characteristics, treatment responses, and toxicities were collected and analyzed.

We identified 13 patients who underwent mogamulizumab retreatment (MF=7, SS=6). The majority were mogamulizumab-responders in their initial exposure (12/13) with 8 complete response (CR), 4 partial response (PR), and 1 stable disease (SD). 5 patients (38.5%) had negative flow cytometry at the time of initial discontinuation. 12/13 patients had MAR with initial treatment, 10 of which were biopsy-confirmed (83.3%).

Median interval from initial mogamulizumab discontinuation to retreatment was 11.4 months (range, 3.1- 40.2). Retreatment dosing schedules included standard dosing (n=2), every-2-weeks (n=8), and every-4-weeks (n=3). On retreatment, ORR was 38.5% (5/13) with 2 CR and 3 PR, and median duration of response was 15 months (range, 0–41). MAR recurred in 10 patients (83.3%), with median onset of 3 months after reinitiation (range, 0.03–40) including biopsy-confirmed in 4 patients (40%). MAR was CTCAE grade≤2 in all patients. MAR was managed with topical steroids (n=9), oral steroids (n=1), and cessation of mogamulizumab (n=9).

Patient	Age at CTCL diagnosis	CTCL subtype	Ref Register Sézary Syndrome treatment courses	Number of months on Mogamulizumab		Dosing interval on retreatment	Onset of rash following Mogamulizumab start (months)		Duration of response (DOR) to Mogamulizumab (months)		Flow cytometry at time of initial discontinuation of Mogamulizumab	Biopsy-confirmed MAR? (Y/N)		MAR location and description	CTCAE grade	BSA involvement of MAR	MAR treatment
				Initial	Retreatment		Initial	Retreatment	Initial	Retreatment		Initial	Retreatment				
1	74	Erythrodermic MF	3	3	3	q2w	No rash	No rash	4	9	Negative	N/A	N/A	No rash	N/A	N/A	No MAR
2	74	SS	2	4	0.03	q2w	1	0.14	4	0	Negative	Yes	No	Maculopapular rash on chest and back	2	60%	Discontinued mogamulizumab; topical steroids
3	69	MF/SS	3	30	26	q2w	32	26	35	29	Positive	Yes	Yes	Initially disseminated, spread to arms, legs, and buttocks; scattered pink thin and scaly macules and papules	2	<10%	Discontinued mogamulizumab; topical steroids
4	49	SS	2	10	5	q2w	9	2	12	6	Positive	Yes	Yes	Pink thin papules and plaques scattered on back and extremities	1	30%	Discontinued mogamulizumab; topical steroids
5	66	SS	3	29.5	4	q2w	3	4	4	6	Negative	Yes	Yes	Erythematous plaques on left chest extending across midline	2	<2%	Topical steroids, oral antibiotics; discontinued mogamulizumab due to cumulative exposure
6	69	MF	2	13.5	42	q4w	10	40	16	43	Positive	Yes	No	Erythematous plaques on lower abdomen, diffuse lesions of trunk and lower extremities	2	10-15%	Topical steroids; space-out mogamulizumab dose
7	57	Erythrodermic MF	2	3	4	q4w	4	0.5	5	4	Negative	Yes	No	Diffuse cosine, scaly plaques over trunk, extremities and buttocks; diffuse erythematous scaly plaques over face and scalp	2	80%	Topical and oral steroids; eventually mogam discontinued and next line of treatment initiated due to progressive disease
8	71	Erythrodermic MF	2	3	2	q2w	6	2	10	0	Negative	No	No (biopsy showed progressive CTCL)	Well-demarcated erythematous scaly plaques on chest and back	Unknown	3-7%	Topical steroids; mogamulizumab discontinued due to progressive disease
9	62	MF	2	3	4	q2w	4	Unknown	Unknown	14	Unknown	Unknown	Unknown	Unknown; CT scans of outside studies	Unknown	Unknown	Discontinued mogamulizumab
10	77	SS	2	10	5	q2w	3	10	9	11	Positive	No	No	Erythematous patches on back and neck	Unknown	Unknown	Discontinued mogamulizumab; topical steroids
11	66	MF	2	4	2	weekly	4	No rash	4	4	Positive	Yes	N/A	No rash	N/A	N/A	No MAR; next line of treatment initiated due to progressive disease
12	62	SS	3	5	0.5	weekly	5	0.03	26	0	Positive	Yes	Yes	Erythematous papules and plaques scattered on upper extremities, trunk, and lower extremities	2	60%	Topical steroids; discontinued mogamulizumab
13	70	MF/SS	2	9.5	5	q2w	10	No rash	27	6	Positive	Yes	N/A	No rash	N/A	N/A	No MAR; discontinued mogamulizumab due to partial remission

Conclusion: In this real-world, heavily pretreated CTCL cohort, mogamulizumab retreatment demonstrated meaningful clinical activity with durable responses. Rash was common but typically low to moderate grade and responsive to standard management. Biopsy was critical in distinguishing MAR from disease progression. Extended-interval dosing may mitigate, but not eliminate, rash-related toxicity, warranting further evaluation.

Learning Objectives:

1. Describe the clinical outcomes and durability of response associated with mogamulizumab retreatment in patients with relapsed/refractory MF and SS following prior treatment discontinuation.
2. Recognize and manage mogamulizumab-associated rash (MAR) upon retreatment, including the potential role of extended-interval dosing to mitigate toxicity while maintaining efficacy.

3B.03 "Moga-Stop" Study: Extended Follow-up of Patients with Sézary Syndrome Treated with Mogamulizumab After Treatment Discontinuation, Excluding for Progression

Oro, Saskia[1], Amatore, Florent[2], El Aarbaoui, Tarik[1], de Masson, Adèle[3], Pham-Ledard, Anne[4], Dereure, Olivier[5], Quereux, Gaëlle[6], Faiz, Sarah[7], de Vicq de Cumptich, Marine[8], Ram-Wolff, Caroline[3], Janela-Lapert, Raphaël[9], Guenova, Emmanuella[10], Lheure, Coralie[11], Le Corre, Yannick[12], Adamski, Henri[13], Bonnet, Nathalie[2], Grange, Florent[14], Troin, Laura[15], Tzoumpa, Sofia[1], Bagot, Martine[3], Beylot-Barry, Marie[4]

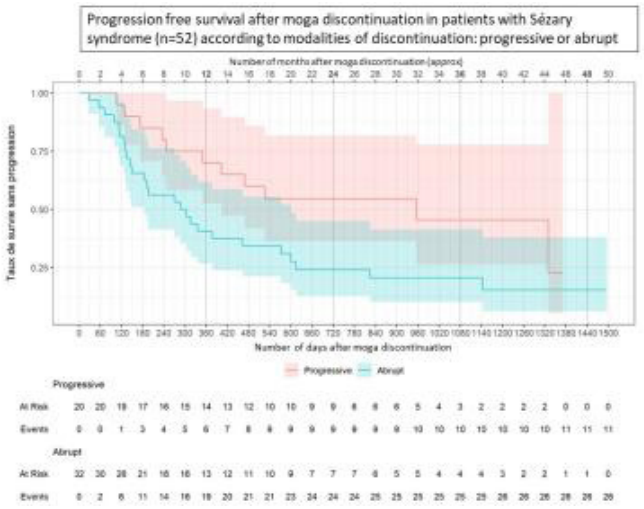
1. Henri Mondor hospital, Créteil, France, 2. Hôpital Nord, Marseille, France, 3. Saint-Louis Hospital, Paris, France, 4. CHU Bordeaux, Bordeaux, France, 5. CHU Montpellier, Montpellier, France, 6. CHU Nantes, Nantes, France, 7. CHU Lille, Lille, France, 8. Saint-Pierre University hospital, Bruxelles, Belgium, 9. CHU Rouen, Rouen, France, 10. CHUV, Lausanne, Switzerland, 11. Cochin Hospital, Paris, France, 12. CHU Angers, Angers, France, 13. CHU Rennes, Rennes, France, 14. CHU Valence, Valence, France, 15. CHU Nice, Nice, France

Introduction: Mogamulizumab (moga) increases progression-free survival (PFS) in Sézary syndrome (SS). After a first study conducted in French cutaneous Lymphoma study group, describing 52 SS patients who discontinued moga for other reasons than progression, we report the extended follow-up data of this cohort.

Methods, Results: We updated the follow-up data for the 47 patients alive after this first study, including 26 in remission. We analyzed PFS after moga discontinuation (pmPFS), resumption of moga for relapse (including safety [moga-associated rash, MAR]) and outcomes. These results were compared to a French cohort of 20 SS patients, treated with moga for at least 12 months, who achieved disease control but for whom the decision was made to continue treatment until progression.

After a median follow-up of 33 months (4-63) after moga discontinuation, 17/52 patients (33%) did not relapse. Median pmPFS was 13 months, significantly longer in patients with gradual discontinuation (p=0.04) (Figure). Among 16 patients who resumed moga for relapse, 8 (50%) achieved CR/PR. Relapse of MAR was unpredictable (3/6 patients with MAR during the initial treatment, sometimes of different aspect). Among the 11 patients who died, only 4 deaths were due to SS. At last report, 31/52 patients (60%) were alive in remission (CR/PR).

In the control cohort (median moga duration was 16 months; median follow-up 32 months), 8 patients experienced MAR, median PFS was 14 months, and 4 patients died of disease.



Conclusion: Prolonged PFS can be achieved in SS after moga discontinuation in patients with an initial good response, with outcomes comparable to responders who continued treatment. Gradual discontinuation appears to improve pmPFS, reducing treatment costs and adverse events. Upon relapse, resumption of moga is effective in 50% of cases and well tolerated. Moga is associated with a low SS-specific mortality in this population (8%).

Learning Objectives:

- Prolonged progression free survival is possible with mogamulizumab in Sézary syndrome, even after discontinuation of the treatment in patients who achieve complete remission;
- Progressive discontinuation is associated to a lower rate of relapse;
- In case of relapse, resumption of mogamulizumab is effective and well tolerated.

3B.04 Overall Survival in Patients with Mycosis Fungoides or Sézary Syndrome in Denmark: Comparative Effectiveness of Mogamulizumab Versus Standard of Care

Morgante, Niccolò[1], Bech, Rikke[2], Rahbek Gjerdrum, Lise Mette[3,4], Kamstrup, Maria R.[5], Skov, Lone[4,6], Madsen, Kristoffer P.[1], Maharaj, Lenushka[7], Specht, Lena[4,8]

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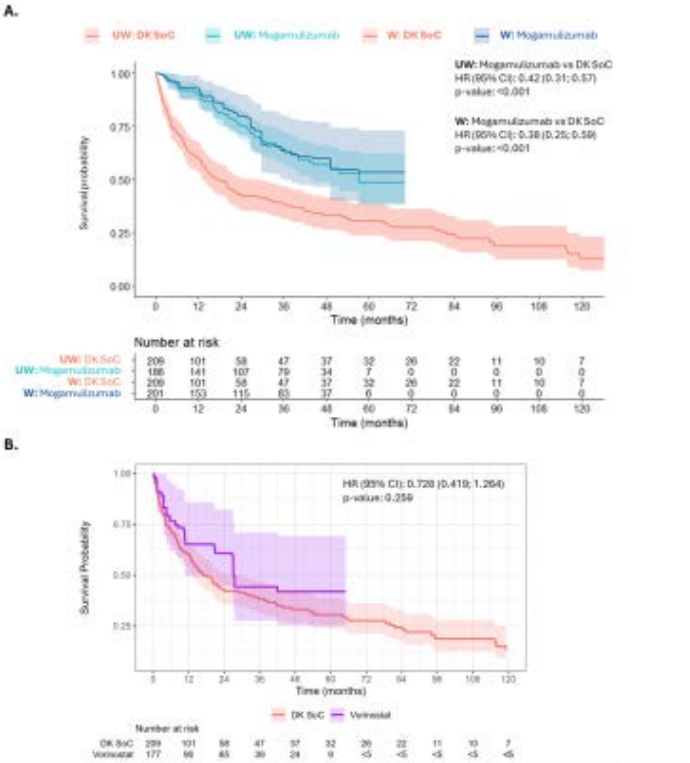
Introduction: Mogamulizumab, authorized by the European Medicines Agency for adult patients with mycosis fungoides (MF) and Sézary syndrome (SS) after ≥1 prior systemic therapy, is not currently recommended in Denmark due to lack of comparative data with Danish Standard of Care (SoC). We evaluated mogamulizumab's effect versus Danish SoC using trial and real-world data (RWD).

Methods, Results: Mogamulizumab data were obtained from the intention-to-treat mogamulizumab arm of the open-label, international, randomized, controlled phase 3 MAVORIC trial (NCT01728805). Danish SoC data, obtained from national registers, included all patients from 1-January-1996 to 15-April-2024 with registered MF/SS diagnosis and ≥1 prior systemic therapy. Individual patient-level MAVORIC data were weighted using a validated inverse probability of treatment weighting approach to match Danish RWD. The comparison was unanchored due to no common comparator. Primary endpoints were Kaplan–Meier estimates of overall survival (OS) (**Figure 1A**). A sensitivity analysis using non-crossover vorinostat data from MAVORIC showed robustness of the weighting method, with no unexpected survival advantage (**Figure 1B**).

Figure 1. Unweighted and ATT-Weighted[a] Kaplan–Meier Curves for OS in Patients Receiving Mogamulizumab Versus Danish SoC (A) and ATT-Weighted Kaplan–Meier Curves for OS in Patients Receiving Vorinostat (B) Versus Danish SoC



[a]n for the weighted (pseudo) populations may be higher than the unweighted (actual) populations.

Abbreviations: ATT, average treatment effect on the treated; DK, Danish; OS, overall survival; SoC, standard of care; UW, unweighted; W, weighted.

Mogamulizumab and Danish SoC populations consisted of 186 and 209 patients, respectively. **Figure 1A** shows Kaplan–Meier OS estimates. Median (95% CI) OS was 57.2 months (44.3–not reached [NR]) and NR (36.6–NR) in the unweighted and weighted mogamulizumab arms, respectively, vs 17.0 months (13.1–29.1) in the Danish SoC arm. The hazard for death was significantly lower for mogamulizumab versus Danish SoC, with a hazard ratio of 0.42 (95% CI: 0.31–0.57; *P*<0.001) unweighted and 0.38 (95% CI: 0.25–0.59; *P*<0.001) weighted, respectively.

Conclusion: This analysis complemented trial data, showing a significantly lower hazard for death with mogamulizumab versus Danish SoC. Since this is a retrospective study, advances in care may explain survival in MAVORIC (from 2014) versus Danish care from 1996. These results support introducing mogamulizumab in adult MF/SS patients after ≥1 prior systemic therapy.

Learning Objectives:

After the presentation, participants will know about potential benefits of mogamulizumab on overall survival in mycosis fungoides and Sézary syndrome based on real-world data.

3B.05 Outcomes in Relapsed/Refractory Mycosis Fungoides or Sézary Syndrome from the MAVORIC Trial Mogamulizumab Arm Versus a Real-world Australian Cohort Receiving Vorinostat

Campbell, Belinda A.[1], Bhullar, Harmeet[1], Jayawardana, Madawa[1], van der Weyden, Carrie[1], Bhabha, Friyana[1], McCormack, Christopher J.[1], Buelens, Odette[1], Chen, Yuxian[2], Linsell, Louise[2], Prince, H. Miles[1]

1. Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, 2. Visible Analytics Ltd., Oxford, United Kingdom

Introduction: Mycosis fungoides (MF) and Sézary syndrome (SS) are rare, potentially debilitating types of cutaneous T-cell lymphoma (CTCL) that have progressively poorer survival with advancing stage. In the phase 3 MAVORIC trial (NCT01728805), patients with relapsed/refractory MF/SS receiving mogamulizumab had significantly longer progression-free survival compared with those receiving vorinostat. However, >70% of patients on vorinostat crossed over to mogamulizumab when permitted by the study protocol, confounding comparison of overall survival (OS). This study used real-world data from patients on vorinostat from an Australian Cutaneous Lymphoma Database (CLD) to estimate the effectiveness of mogamulizumab relative to vorinostat.

Methods, Results: Unanchored matching-adjusted indirect comparisons were performed. Individual patient data from MAVORIC (mogamulizumab arm) were reweighted on age group, sex, histology, disease stage at treatment initiation, and Eastern Cooperative Oncology Group performance score to match the baseline characteristics of the vorinostat cohort. Hazard ratios (HRs) were estimated using a Cox regression model.

186 patients who received mogamulizumab (MAVORIC) were compared with 67 patients receiving vorinostat (CLD). Following reweighting, median OS was not reached for mogamulizumab (N=42; median follow-up 37.6 months, 95% CI 35.3–41.6) and was 31.0 months (95% CI 21.1–41.2) for vorinostat (median follow-up 58.1 months, 95% CI 46.8–non-estimable); patients treated with mogamulizumab had significantly longer OS (HR 0.23; 95% CI 0.12–0.43; p<0.001) (Figure). Median time to next treatment was numerically longer for mogamulizumab (11.53 months; 95% CI 6.80–20.57) compared with vorinostat (5.82 months; 95% CI 3.76–7.67; HR 0.62; 95% CI 0.36–1.06; p = 0.083).

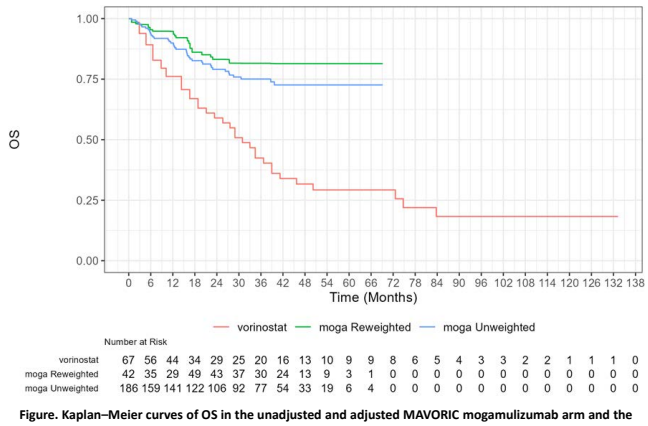


Figure. Kaplan–Meier curves of OS in the unadjusted and adjusted MAVORIC mogamulizumab arm and the CLD vorinostat cohort

Conclusion: In rare diseases like CTCL with significant unmet need, treatment cross-over during trials often complicates comparison of long-term outcomes. By leveraging real-world data to overcome

this limitation, our findings add to the growing evidence suggesting that mogamulizumab may provide an OS benefit compared with vorinostat for patients with relapsed/refractory MF/SS.

Learning Objectives:

- Participants will understand how statistical adjustments can be made between trial and real-world data to compare treatments in situations where longer-term outcomes cannot be compared using trial data due to treatment crossover.
- Participants will understand the improvement in OS with mogamulizumab relative to vorinostat estimated using a model that adjusted the characteristics of patients with MF/SS in the mogamulizumab arm of MAVORIC to more closely match a cohort receiving vorinostat from a real-world database.

SESSION 4A: CONTEMPORARY ADVANCES IN CUTANEOUS T-CELL LYMPHOMAS: NEW FRONTIERS IN CUTANEOUS LYMPHOMA DIAGNOSIS AND PROGNOSIS

4A.01 Presentation with Confluent Erythema Not Reaching 80% Body Surface Area is Associated with Advanced Stage Disease and Has Worse Outcome Than Classical MF in the Early Stages

Scarisbrick, Julia J.[1,2], Bashir, Abraham E.[1,2], Evision, Felicity[1], Gru, Alejandro A.[3], Papadavid, Evangelia[4], Kim, Youn H.[5], On behalf of PROCLIPI collaborators

1. University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, 2. University of Birmingham, Birmingham, United Kingdom, 3. Columbia University Irving Medical Center, New York City, NY, USA, 4. National and Kapodistrian University of Athens, Athens, Greece, 5. Stanford University School of Medicine, Palo Alto, CA, USA

Introduction: Erythroderma is defined by >80% body surface area (BSA) erythema but some CTCL patients skin involvement falls short of this %BSA. The term 'confluent erythema' may be used to describe patients with areas of erythema which may be indurated but without clear demarcation from normal skin differentiating this from patches and plaques which may coalesce. The presence of confluent erythema is recorded in the PROCLIPI study(ClinicalTrials.Gov ID:NCT02848274).

Methods, Results: We interrogated the PROCLIPI database to identify patients with confluent erythema and BSA<80%. 137 (12.6%,n=1091) were recorded clinically as having confluent erythema with a median follow-up of 5.4 years (95%CI:4-6.25). Patients are older 66 (IQR: 55,72) than those without confluent erythema 59 (IQR:46,70);p=0.0002 and more likely to be advanced stage at diagnosis 56.2) vs 23.0%;p<0.001. Median total mSWAT is 50 (IQR:26,72,range:1,170). Median BSA involved is 40% (IQR:18,64,range:0.7,79,mean=40.3,mode=60).

B stage at diagnosis was not recorded in 42.3%, 39.3%= B0, 12.7%=B1 and 49.1%=B2. N stage at diagnosis was not recorded in 20.4%, 78.9%=N0, 8.3%%=N1, 0%=N2 and 12.8%= N3. Overall stage was early in 60 patients; IA=14 (10.2%), IB=37 (27.0%), IIA=9 (6.6%) and advanced in 77 patients; IIB=16 (11.7%), IVA1=45 (32.9%), IVA2=12 (8.8%), and IVB in 4 (2.9%).

15/60 (25%) patients progressed from early to advanced during median follow-up of 5.4 years months compared to 8.6% or classical early MF patients. The OS of the early and advanced cohort were 96.4%,84.4% 1yr, 90.1%,64.4% 3yr and 71.7%,48.0% 5yr-survival.

Conclusion: Over half of patients with confluent erythema but not reaching erythroderma >80% had advanced stage MF. Nearly 50% had B2 and 13% had N3. Patients with MF with confluent erythema had a worse outcome than classical MF (Fig 1, p<0.001) and were more likely to progress to advanced disease. This data highlights the need to perform blood flow and nodal examination in this subset of patients.

Learning Objectives:

1. Recognise and define confluent erythema in cutaneous T-cell lymphoma (CTCL) and distinguish it clinically from classical patches, plaques, and erythroderma.
2. Assess the prognostic and staging implications of confluent erythema in mycosis fungoides, including its association with advanced stage disease, blood (B) and nodal (N) involvement, and risk of progression.
3. Apply evidence from the PROCLIPI study to clinical practice by identifying CTCL patients with confluent erythema who warrant comprehensive staging, including blood flow cytometry and nodal assessment.

4A.02 Cutaneous Flow Cytometry: 10 Years of Experience from a Single Center

Martins, Francisco[1], Paiva, Artur[2], Guenova, Emmanuella[3], Cardoso, José Carlos[1], Calvão, Joana[1]

1. Dermatology Department, University Hospital, Local Health Unit of Coimbra, Coimbra, Portugal, 2. Flow Cytometry Unit, Local Health Unit of Coimbra, Coimbra, Portugal, 3. Department of Translational Immunodermatology, Kepler University Hospital, Johannes Kepler University, Linz, Austria

Introduction: Cutaneous lymphomas and cutaneous infiltrations by systemic hematologic neoplasms represent one of the greatest diagnostic challenges in Dermatology, requiring close correlation between clinical, histological, and laboratory findings. Cutaneous flow cytometry (CFC) allows rapid immunophenotyping of aberrant cell populations; however, its use in routine clinical practice is uncommon, and large-scale retrospective studies are scarce.

Methods, Results: All CFC immunophenotyping (IFP) examinations performed at a hospital centre over a 10-year period (2015–2025) were included. Demographic and clinical data were collected, including the initial diagnostic suspicion and final diagnosis. The rate of conclusive examinations (defined as the presence of sufficient cells for analysis) was assessed. In addition, the diagnostic performance of CFC in distinguishing cutaneous lymphomas and secondary cutaneous infiltrations by systemic hematologic neoplasms from non-hematologic lesions was evaluated by calculating sensitivity, specificity, and accuracy. Statistical analysis was performed, using tests for comparison of proportions when appropriate.

A total of 301 IFP examinations from 266 patients were analyzed (56% male; mean age 63 years). CFC was conclusive in 77.1% of non-hematologic lesions, 88.4% of indolent cutaneous lymphomas, 92.3% of aggressive cutaneous lymphomas, and 93.5% of secondary infiltrations (χ^2 (3) = 8.652; p = 0.034). Among conclusive examinations, CFC showed a sensitivity of 67.7%, specificity of 92.2%, and accuracy of 81.9% for the detection of neoplastic hematologic infiltrates. In the detection of high-grade neoplasms (aggressive cutaneous lymphomas and secondary infiltrations), sensitivity was significantly higher (87.3%; p < 0.01). In cases of initial diagnosis, when positive, CFC anticipated the diagnosis by a mean of 25 days.

Conclusion: Cutaneous flow cytometry immunophenotyping proved useful in detecting neoplastic hematologic infiltrates, particularly aggressive cutaneous lymphomas and cutaneous infiltrations by systemic hematologic neoplasms, and may allow earlier diagnosis.

Learning Objectives:

After this presentation, participants will be able to:

1. Understand the diagnostic value of cutaneous flow cytometry in the detection and immunophenotypic characterization of cutaneous neoplastic hematologic infiltrates.
2. Recognize the clinical scenarios in which cutaneous flow cytometry can anticipate or improve diagnosis, in patients with suspected cutaneous hematologic disease.

4A.03 Reproducible Cohort Generation and Whole-Slide Learning for Cutaneous T-Cell Lymphoma and Related Lymphoproliferative Disorders

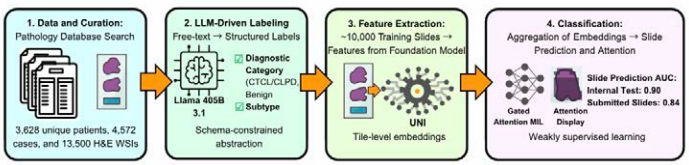
Kamali, Ali[1], Goldgof, Greg[1], Vanderbilt, Chad[1], Yin, Neo[2], Ardon, Orly[1], Moy, Andrea[1], Dogan, Ahmet[1], Pulitzer, Melissa[1]

1. Memorial Sloan Kettering Cancer Center, New York, NY, USA,
2. University of California, Berkeley, Berkeley, CA, USA

Introduction: Cohort definition in cutaneous T-cell lymphoma and related cutaneous lymphoproliferative disorder (CTCL/CLPD) studies often relies on implicit criteria and ad-hoc manual curation. Current approaches have limited reproducibility and hindering cross-study comparison with downstream consequences for diagnosis, treatment, and prognostication. Furthermore, building robust clinical-use histopathology AI for CTCL/CLPD requires large, diverse, richly labeled whole-slide datasets, which are infeasible to curate manually.

Methods, Results: We developed an end-to-end workflow that integrates report abstraction using a large language model (LLM) with weakly supervised learning on whole-slide images (WSIs), with iterative dermatopathologist validation. The LLM converts narrative reports into structured slide-level labels (diagnostic category/subtype, likelihood qualifiers, and tissue-site attribution), capturing decision logic without manual region annotation or external chart review. For classification of hematoxylin and eosin (H&E) WSIs, we extracted tile embeddings using a pretrained pathology foundation model and aggregated them with gated-attention multiple instance learning (MIL). We evaluated performance on a held-out, pathologist-verified internal test set and an external cohort of slides submitted from outside institutions but scanned locally.

LLM-driven curation identified 13,500 WSIs scanned at 20x and 40x derived from 3,628 patients spanning 7 CTCL/CLPD subtypes and 12 benign inflammatory diseases (BID). On a pathologist-verified subset, diagnostic category assignment achieved weighted accuracies of 94.4% for CTCL/CLPD and 98.0% for BID. The slide-level classifier achieved ROC–AUC 0.898 (95% CI, 0.874–0.919) and accuracy 0.82 on the internal test set (814 slides; sensitivity 0.76, specificity 0.85), and generalized to externally submitted material despite heterogeneous staining (ROC–AUC 0.839). Attention maps highlighted meaningful regions without region-level supervision.



Conclusion: Schema-guided LLM report abstraction enables reproducible, diagnostically granular CTCL/CLPD/BID cohort generation while providing scalable supervision for whole-slide learning. Paired with weakly supervised MIL, this traceable decision-modeling approach supports robust, transparent slide-level classification from routine H&E WSIs, with potential utility for research, ancillary study triage, quality assurance, and second-opinion support.

Learning Objectives:

1. Participants should be able to explain how a traceable decision modeling approach improves the ability to scale reliable cohorts of CTCL/CLPD/BID for research on disease subsets.
2. Based on this work, participants should be able discuss how schema guided LLM report abstraction with weakly supervised MIL can be implemented for a work-flow based stratification of CTCL/CLPD/BID.
3. Participants should be able to appraise the potential accuracy of expert pathologist-verified LLM curation with weakly supervised MIL for CTCL/CLPD/BID diagnostic category assignment in the absence of clinical charts or manual annotation of slides.

4A.04 Investigating the Genetic Landscape of Primary Cutaneous Lymphomas and Lymphoproliferative Disorders with T Follicular Helper Cell Phenotype (PCL-TFH)

Rahbar, Ziba[1], Melendez, Brenda[2], Fong, Lon Wolf[2], Huen, Auris[2], Cho, Woo C[2], Nagarajan, Priyadharsini[2], Aung, Phyu P.[2], Dai, Julia[2], Curry, Jonathan L.[2], Prieto, Victor G.[2], Iyer, Swaminathan[2], Lazcano, Rossana[1], Miranda, Roberto N.[2], Wargo, Jennifer[2], Lazar, Alexander J.[2], Torres-Cabala, Carlos A.[2]

1. Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA,
2. The University of Texas, MD Anderson Cancer Center, Houston, TX, USA

Introduction: Primary cutaneous lymphoid proliferations with T follicular helper (TFH) phenotype overlap with CD4+ small/medium T-cell lymphoproliferative disorder (CD4+SMLPD), rare mycosis fungoides/Sézary syndrome (MF/SS), and secondary skin involvement by nodal TFH lymphoma (AITL). We previously identified a cohort of PCL-TFH lacking typical features of these entities and demonstrating variable clinical outcomes. We aimed to define their spatial transcriptomic signatures and differentiating molecular markers.

Methods, Results: Cases meeting TFH phenotype by immunohistochemistry (≥2 of PD-1, CXCL13, ICOS, BCL6, CD10) with available tissue blocks were assembled into tissue microarrays, including comparator cohorts (CD4+SMLPD, AITL, and rare MF with TFH-phenotype). Spatial transcriptomics was performed on formalin-fixed, paraffin-embedded sections using GeoMx Digital Spatial Profiling with tumor and microenvironment segmentation. We conducted all sample processing, library preparation, sequencing (NovaSeq 6000), and downstream transcriptomic/statistical analyses. Differential expression and marker discovery were modeled using GOMix linear mixed-effects frameworks, accounting for repeated measures and segment type.

Fifteen patients (70 biopsies) were analyzed: 7 with TFH phenotype (PCL-TFH), 3 with AITL, 3 with MF, and 2 with CD4+SMLPD. Among the TFH group, 9 biopsies came from patients with stable skin-limited disease (Category 1), and 8 from those with systemic progression (Category 2); three patients died. After QC, 126 segmented ROIs were retained (10,200 genes). Tumor segments demonstrated a TFH-activated T-cell program enriched for *TRAC*, *TRBC1*, *CD3D*, *ICOS*, *TOX*,

IL32, *LAT*, and *SLA*. Microenvironment segments were enriched for vascular–stromal/ECM genes (e.g., *PECAM1*, *TM4SF1*, *COL4A2*, *LAMC1*, *SPARCL1*). Differences between outcome groups localized to the microenvironment: Category 1 showed higher *EIF4B*, *MAP3K1*, *GLIPR1*, *PIK3CG*, *SECISBP2*, and *SP3* (FDR < 0.05). Pooled modeling further identified *SEC62* and *UXT* enriched in Category 1, and *SGCB* and *C17orf58* in Category 2. No tumor-compartment genes significantly differed.

Conclusion: PCL-TFH exhibits shared TFH-activated tumor program with outcome-associated differences confined to the microenvironment. Spatial profiling may support refined classification and risk-informed monitoring.

Learning Objectives:

1. Recognize the clinicopathologic setting of PCL-TFH.
2. Describe key tumor-compartment and microenvironment markers identified by GeoMx analysis in PCL-TFH.
3. Discuss how spatial transcriptomic signatures may support classification and monitoring for systemic progression.

4A.05 Co-occurring Chronic Lymphocytic Leukemia in Mycosis Fungoides/Sézary Syndrome: Retrospective Analysis

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Introduction: Chronic lymphocytic leukemia (CLL) has been frequently reported as a co-occurring malignancy in patients with mycosis fungoides (MF) and Sézary syndrome (SS). We aimed to investigate whether the presence of CLL influences the disease severity of patients with MF/SS.

Methods, Results: We utilized the MD Anderson Cancer Center (MDACC) Retrospective Database of Cutaneous Lymphomas, which includes 3,267 patients with MF/SS who were seen and/or treated at our institution between January 1987 and May 2024, to identify MF/SS patients with concomitant CLL.

We identified 51 patients with concomitant CLL and MF/SS, including 11 patients with SS, representing 1.5% of the entire cohort. The cohort included 21 females (41.2%) and 30 males (58.8%). The majority were White (46, 90.2%). Of the 51 patients; 27 were diagnosed with CLL prior to MF/SS, 14 were diagnosed within 6 months of MF/SS diagnosis, and 10 were diagnosed more than 6 months after MF/SS. Overall, 56.8% of patients had advanced-stage MF/SS: IIB (10, 19.6%), IIIA (2, 3.9%), IVA1 (8, 15.7%), IVA2 (4, 7.8%), and IVB (5, 9.8%). Among the 10 patients whose CLL was diagnosed more than 6 months after MF, 4 (40%) had advanced-stage MF/SS, whereas among the remaining 41 patients, 25 (60.9%) had advanced-stage disease.

Conclusion: CLL was observed at a rate of 1.5% in our MF/SS cohort. We observed a high proportion of advanced-stage disease in MF/SS patients with concomitant CLL, with even higher rates among those with preceding CLL. These findings suggest that the presence of CLL may be associated with a more aggressive disease course in MF/SS patients.

Learning Objectives:

CLL can be seen as a co-occurring malignancy in MF/SS patients, with this association noted more frequently among White patients. The coexistence of CLL may be associated with more severe disease in MF/SS.

4A.06 Non-alpha/beta T-Cell Lymphoma: a Single Centre Experience on Gamma/Delta and TCR-Silent Subsets

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Introduction: Within non-alpha/beta proliferations, gamma/delta+ cutaneous T-cell lymphomas (CTCL) are formally recognized, but a T-cell receptor (TCR)-silent phenotype (non-alpha/beta and non-gamma/delta) can be encountered, as an elusive subtype.

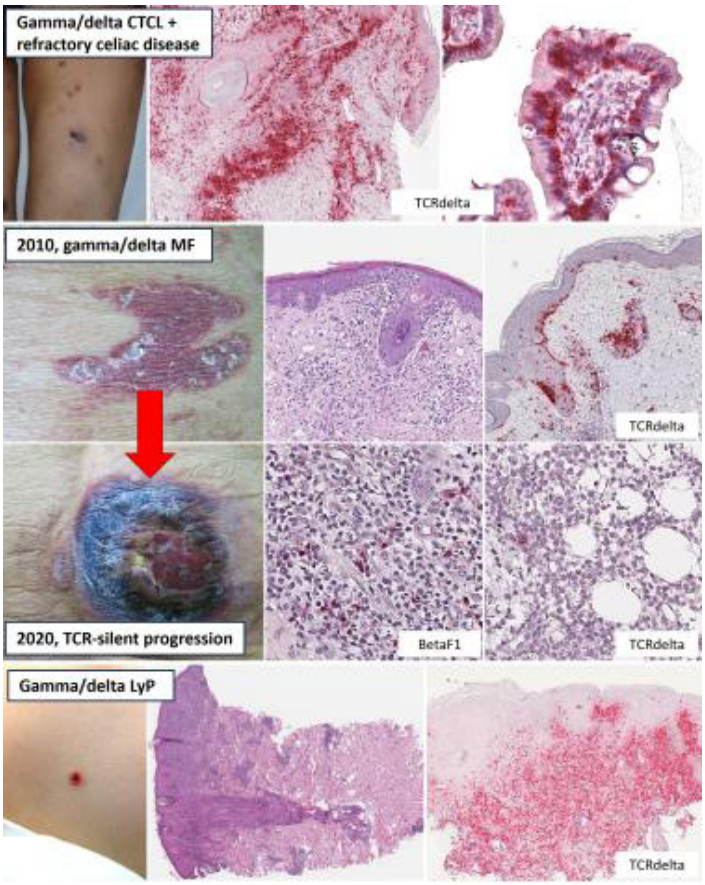
Methods, Results: Retrospective, continue series of CTCLs routinely diagnosed from 2019 to 2024 and followed at a single Institution, featuring either a BetaF1-/TCRdelta+ or BetaF1-/TCRdelta-, EBV-negative phenotype, and demonstrating monoclonal *TCRG* rearrangement (BIOMED-2).

36 patients: 25 gamma/delta and 11 TCR-silent, over a median follow up of 33 months (range 7-240).

Gamma/delta subset: Eight patients featured panniculitis-like gamma/delta-CTCL, with tendency to aggressive behavior (3 died-of-disease; median follow-up 17 months), one patient featuring coexistent refractory celiac disease, with gamma/delta+ duodenal lymphocytosis, one shifting to TCR-silent phenotype.

Ten patients presented with the clinic-pathologic profile typical of mycosis fungoides (MF), all alive with disease (median follow-up 84 months), except for one progressing to tumor-stage, TCR-silent CTCL after a 12-year follow-up. Six patients (median age: 9 years) featured typical lesions and behavior of lymphomatoid papulosis (LyP). One patient displayed a CD4+/TCRdelta+ proliferation, with a clinic-pathologic profile recapitulating Sézary syndrome.

TCR-silent subset: Two cases demonstrated pleomorphic, dermal-hypodermal TCL, with rapid progression to systemic, non-nodal disease. One patient presented a MF-type picture (follow up: 17-years). Remaining cases fell within typical CD30+ lymphoproliferative disorders (LPD), including seven LyP (two of which, CD30-negative) and one primary cutaneous anaplastic large cell lymphoma (pcALCL).



Conclusion: Our experience stresses that gamma/delta-CTCLs encompass a broad clinicopathological spectrum, including indolent variants that challenge the conventional prognostic framework. Outside the boundaries of LyP/pcALCL, they also stand in a continuum with TCR-silent CTCLs, with tendency to progressive/aggressive course.

For diagnostic purposes, TCR-silent phenotype is proper to CD30+ LPD/lymphomas, which share a heavily disrupted T-cell differentiation (PMID:20511667), but it is also observed in aggressive, extranodal TCL (PMID:21753698).

Classification of CTCL is a matter of clinic-pathologic pattern, rather than adherence to strict criteria.

Learning Objectives:

1. To discuss the clinic-pathologic picture of primary cutaneous T-cell lymphomas featuring a non alpha/beta phenotype
2. To discuss the challenges and the grey zones in the current cutaneous lymphoma classifications

4A.07 Mycosis Fungoides with a Gamma-Delta Immunophenotype: Do They Differ from Epidermotropic Primary Cutaneous Gamma-Delta T-Cell Lymphoma?

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Introduction: Mycosis fungoides (MF) cases with a gamma-delta phenotype are classified under MF per current guidelines. However, some of these cases may progress to cytotoxic lymphoma, suggesting that such cases should be classified as primary cutaneous epidermotropic gamma-delta T-cell lymphoma (PCGDTCL). We evaluated gamma-delta MF (gdMF) cases at our institution from 2010-2025 and extracted demographics, histopathological phenotype, and clinical course to identify predictors indicative of progression to cytotoxic lymphoma.

Methods, Results: All patients (n =34; M:F, 1.4:1) presented with patches/thin plaques (31/34) or erythroderma (3/34) without tumors, ulceration, or systemic involvement. The median time from disease onset to presentation was 6 years (IQR, 11.5; range, 0.1-46 years), and the median age of diagnosis was 61 (range: 16-87) years. With a median follow-up of 4.3 (6.4; 0.1-28) years, 29 patients were indolent, while 5 patients progressed to cytotoxic lymphoma, with ulcerated tumors/thick plaques (n = 5), nodal involvement (n = 3), and/or metastases (n = 3). Cytotoxic patients were older with shorter duration of symptoms and more extensive skin involvement at presentation; they were also more likely to have head/neck or peri-mucosal involvement (p<0.01).

Histopathologic evaluation demonstrated rare necrotic keratinocytes in 15/34 cases (cytotoxic, 3/5 cases) and visible adnexa in 26/34 cases. Six cases were truly folliculotropic (cytotoxic, 2/5 cases), while 5 had mild folliculotropic infiltrate. Regarding phenotype, most patients were double-negative (CD4-/CD8-, 22/34; CD8+, 6/34; CD4+, 5/34; CD4+/CD8+, 1/34). For the patients that progressed to cytotoxic lymphoma, 3 were CD4-/CD8- and 2 were CD4+. No patients had large cell transformation (LCT) at presentation; however, 4/5 patients that progressed developed LCT in later biopsies.

Demographic and clinical characteristics of gamma-delta mycosis fungoides.

Clinical Characteristics	Entire Cohort	Cytotoxic/ transformed patients	Indolent patients	
N	34	5	29	
Mean age at diagnosis, years	57	65	56	
Sex (N, %)				
	Male	20 (59)	3 (60)	17 (59)
	Female	14 (41)	2 (40)	12 (41)
Race (N, %)				
	White	20 (65)	4 (80)	16 (62)
	Black	6 (19)	1 (20)	5 (19)
	Other	5 (16)	0 (0)	5 (19)
FST (N, %)				
	Light (I-III)	23 (72)	4 (80)	19 (70)
	Dark (IV-VI)	9 (28)	1 (20)	8 (30)
Duration of Symptoms Prior to presentation in Years (median, IQR, range)	6 (11.5; 0.1-46.0)	4 (0.5; 3.0-5.0)	8 (12.5; 0.1-46.0)	
Length of follow-up (median, IQR, range) (years)	4.3 (6.4; 0.1-28.0)	7.1 (3.5; 4.7-11.0)	3.5 (7.0; 0.1-28.0)	
Total disease duration (median, IQR, range) (years)	11.4 (11.6; 0.6-48.1)	10.6 (2.6; 8.7-16.0)	15.3 (12.9; 0.6-48.1)	

Stage at Diagnosis (N,%)				
	IA	17 (52)	2 (40)	15 (54)
	IB	13 (36)	3 (60)	10 (36)
	IIA-IIB	0	0	0 (0)
	IIIA-IIIB	3 (9)	0 (0)	3 (10)
Status (N, %)				
	Alive	29 (85)	1 (20)	28 (97)
	Dead	5 (15)	4 (80)	1 (3)

Conclusion: Our work suggests that gdMF has a more indolent course than other gamma-delta lymphomas. Older age at presentation and peri-mucosal/head-and-neck involvement were the only factors significantly associated with progression to cytotoxic lymphoma.

Learning Objectives:

1. Participants should recognize basic clinical and histological features of gamma-delta mycosis fungoides.
2. Participants should recognize that gamma-delta mycosis fungoides has a more indolent course than other gamma-delta lymphomas.

SESSION 4B: INTEGRATING IMMUNE PROFILING WITH GENOMICS TO PREDICT THERAPY RESPONSE

4B.01 Functional Immune States of Blood and Skin Microenvironment Predict Mogamulizumab Response in Sézary Syndrome

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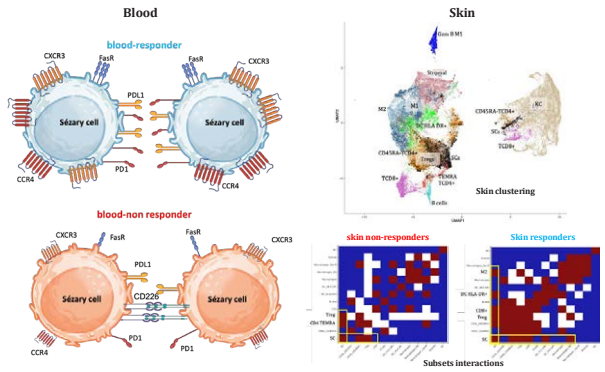
Introduction: Defining tumor and microenvironment (TME)-related determinants of mogamulizumab response is critical for patient stratification and elucidating mechanisms of skin homing, intercompartmental trafficking, and resistance. We conducted an integrative study using multi-parametric flow cytometry (FC) and imaging mass cytometry (IMC) with spatial profiling to characterize tumor-cells and their blood and skin microenvironments in relation to compartment-specific responses to mogamulizumab.

Methods, Results: Sézary syndrome (SS) patients were enrolled at baseline with mogamulizumab treatment. Analyses were performed according to blood and skin responses(1). FC used a 29-color panel with TRBC1-based clonality assessment of putative SS cells(2). Unsupervised clustering and dimensionality reduction were performed with CATALYST. IMC was performed on formalin-fixed, paraffin-embedded skin biopsies using a 36-marker panel. Tissue segmentation and single-cell mask generation were generated using Visiopharm® software followed by cellular neighborhoods and spatial community analyses.

Blood response was associated with potentially less aggressive SCs (PD-L1+CD95/FAS+), controlled by T-cells which harbor strong skin homing capacities. Our data suggest that a blood-skin immune continuum promotes therapeutic response by enabling the recruitment of blood-derived effector T-cells and fostering broad interactions among resident immune cells and keratinocytes within a compartment enriched for markers of skin integrity and immune activation, involving integrin and signaling lymphocytic activation molecules (SLAM).



Conclusion: Together with the findings of Phillips et al(3) on immune checkpoint inhibitor responses, our data indicate that a pre-existing functionally competent immune state involving both immune and tumor cells characterizes a subset of patients responding to mogamulizumab. Whether this state represents a general determinant of response remains to be established, particularly in depleting, rather than immunomodulatory, therapeutic settings.

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2. V. A. Ta, *et al.*, *Journal of Investigative Dermatology* (2025).
3. D. Phillips, *et al.*, *Nat Commun* **12**, 6726 (2021).

Learning Objectives:

1. Immune profile characterized by immune T-cells with strong skin homing capacities and potentially less aggressive SCs predict blood response to mogamulizumab
2. Skin environment enriched for markers of skin integrity and immune activation predicts blood response to mogamulizumab.
3. A pre-existing blood–skin immune continuum promotes therapeutic response to mogamulizumab

4B.02 Targeted Sequencing in Patients with Relapsed/Refractory Mycosis Fungoides or Sézary Syndrome Treated with Mogamulizumab in the MOGA-2MG-Q4W Clinical Trial

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Introduction: Cutaneous T-cell lymphomas (CTCL), including mycosis fungoides (MF) and Sézary syndrome (SS), are characterized by heterogeneous somatic mutations in genes encoding epigenetic regulators, T-cell receptor (TCR)/immune signaling genes, and tumor suppressors. These alterations influence clinical response to immunotherapies such as mogamulizumab, a CCR4-targeting antibody.

Methods, Results: Custom-targeted sequencing was performed on responder and non-responder pre- and post-treatment tumor biopsies from the MOGA-2MG-Q4W trial (NCT04745234) to define genomic alterations associated with response to mogamulizumab in relapsed/refractory MF/SS after ≥1 prior systemic therapy.

Sequencing revealed a wide-range of somatic mutational burden across all tested patients. High-frequency mutations such as *FAT1*, *FAT3*, *PCLO*, *TET2*, and *CTLA4* were common in both responders (complete/partial response) and non-responders (stable/progressive disease), consistent with previously reported core CTCL drivers rather than predictors of therapeutic sensitivity. There were distinct trends between responders (n=10) vs non-responders (n=15). Responders harbored mutations in *CREBBP*, *CD28*, *IL2RA*, *MAPK1*, and *ZEB2/ZEB3*, suggesting enhanced immunologic signaling or increased vulnerability to CCR4-directed depletion. Non-responder-enriched mutations were in *MAGI1, EPB41L3, L3MBTL4, NCOR1*, *CDKN2A*, *IRF4*, *BRD9*, *CSNK1A1*, *JAK3*, *JUNB*, and *CARD11* genes indicating potential resistance pathways involving impaired transcriptional regulation, TCR signaling alterations, or enhanced cell-survival programs.

MF and SS skin lesion biopsies revealed differences aligned with known biology, irrespective of response to mogamulizumab. MF showed enrichment of mutations in epigenetic and chromatin-regulatory genes (*MAGI1*, *KMT2B*, *L3MBTL4*, *EPB41L3*), linked to immune evasion, correlating with mogamulizumab resistance. SS exhibited immunoregulatory mutations in *CD28* genes, potentially associated with enhanced antibody-dependent cellular cytotoxicity, correlating with mogamulizumab-mediated response.

Conclusion: In this study, genomic alterations associated with response to mogamulizumab were investigated. Mutations identified in MF might determine resistance through immune evasion. Mutations identified in SS might determine response through $CCR4^+$ malignant and regulatory T-cell depletion enhancing $CD8^+$ T-cell expansion and antitumor immunity. These potential novel predictive and resistance-associated somatic biomarkers may inform personalized treatment decisions.

Learning Objectives:

After viewing this presentation, the learner will be able to describe mutation patterns in patients with mycosis fungoides or Sézary syndrome at baseline and after treatment with mogamulizumab.

4B.03 Rapid and Durable Blood Remission in CTCL Using Mogamulizumab: B2 as a Surrogate Marker

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Introduction: Mogamulizumab, a CCR4 monoclonal antibody, has been approved in Germany since 2020 as second-line therapy for mycosis fungoides (MF) and Sézary syndrome (SS). However, data on optimal treatment duration and interval prolongation remain limited.

Methods, Results: We prospectively monitored **20 CTCL patients with B2 blood involvement** (SS, n = 16; MF, n = 4; stages IVA1–IVA2) using **serial flow cytometry (FACS)** to quantify CD3+, CD4+CD7-, and CD4+CD26- T-cell populations. In a subset of patients, **molecular monitoring of T-cell receptor (TCR) beta and gamma rearrangements** was performed.

Mogamulizumab induced a **rapid and profound reduction of aberrant T-cell populations**, with marked decreases observed early during treatment. Based on best response during the first cycle, **17/20 patients (85%) achieved complete remission, 1/20 (5%) partial response, and 2/20 (10%) progressive disease**. **B0 conversion** was achieved in **19/20 patients (95%)**, indicating effective clearance of the malignant blood compartment. In **7/20 patients**, longitudinal TCR analyses demonstrated a **consistent decline of the malignant T-cell clone**, supporting the FACS-based response assessment. Treatment **interval prolongation** was implemented in **9/20 patients (45%)**, predominantly after stable B0 conversion, with dosing intervals extended to **4–8 weeks** (up to 12 weeks in selected cases). **Mogamulizumab-associated rash (MAR)** occurred in **8/20 patients (40%)** and was associated with treatment adaptations in some cases. Despite deep initial responses, **10/20 patients (50%) required re-treatment**, including **2 patients (10%) receiving three cycles**, most commonly after relapse following treatment discontinuation. The **median treatment-free interval between cycles was 13.9 months** (range 2.5–49.4 months).

Conclusion: CTCL patients with B2 blood involvement show **rapid and durable hematologic responses** to mogamulizumab. A **response-adapted maintenance strategy with interval prolongation after B0 conversion appears feasible**, provided that **close longitudinal monitoring using FACS and molecular TCR analysis** is performed, enabling **clinically meaningful treatment-free intervals exceeding one year** in a substantial proportion of patients.

Learning Objectives:

Treatment-free intervals, Surrogate Marker, TCR

4B.04 Distinct Genomic Profiling of Folliculotropic Mycosis Fungoides: Integrated Data of Whole Genome Sequencing and Single-Cell Spatial Transcriptomics

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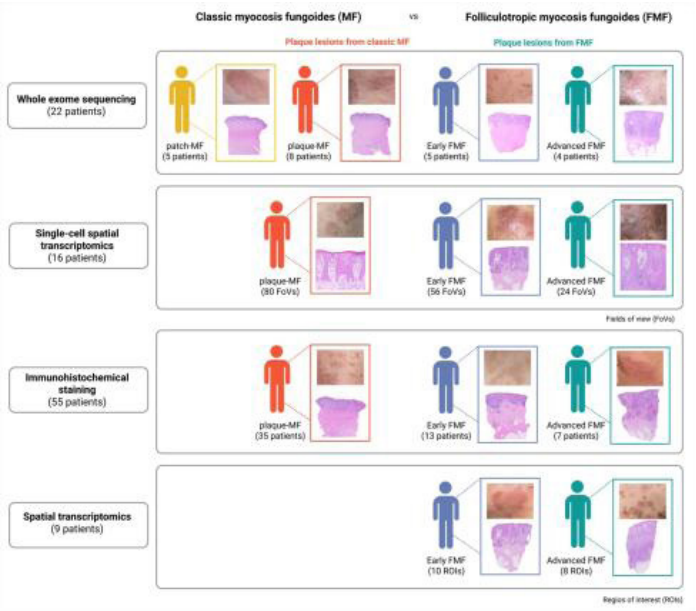
Introduction: Folliculotropic mycosis fungoides (FMF), the most common MF variant, is associated with poorer outcomes compared with stage-matched classic MF. A novel FMF-specific staging system has suggested to distinguish early from advanced FMF, but the biological basis of its unfavorable prognosis remains unclear. This study aims to delineate the molecular landscape of FMF compared to classic MF and clarify genomic and transcriptomic differences underlying its aggressive behavior.

Methods, Results: We analyzed FMF with plaque lesions and classic MF using whole-genome sequencing and single-cell spatial transcriptomics, and subclassified FMF as early or advanced according to the novel staging system. Validation was performed with immunohistochemistry and digital spatial profiling.

Mutational profiles were similar between FMF and classic MF; however, advanced FMF showed higher tumor mutational burden with a C>T/G>A signature. Single-cell spatial transcriptomics, CosMx identified upregulated DEGs, notably CCL17, in folliculotropic T cells from FMF compared with epidermotropic T cells from plaque MF. CCL17 expression was enriched in macrophage–dendritic cell subsets, proinflammatory fibroblasts, and T-cell clusters, with spatial localization around follicles. Cell–cell interaction analysis highlighted MIF–CD74 and CCL17/CCL18–ACKR1 signaling unique to FMF. Across CosMx, immunohistochemistry and digital spatial profiling, CCL17 was consistently elevated in advanced FMF compared to early FMF.



Conclusion: This study establishes distinct molecular features of FMF at DNA and RNA levels and confirms their relevance in advanced disease using an FMF-specific staging system. These findings provide insight into the poor prognosis of FMF and a potential foundation for FMF-targeted therapies.

Learning Objectives:

1. To understand the tumor microenvironment of folliculotropic mycosis fungoides.
2. To understand the genomic and transcriptomic differences that may explain the aggressive behavior of folliculotropic mycosis fungoides.

4B.05 Non-JAK-Family Gene Fusions in Cutaneous T-cell Lymphoma Highlights Genetic Diversity and Potential Therapeutic Targets

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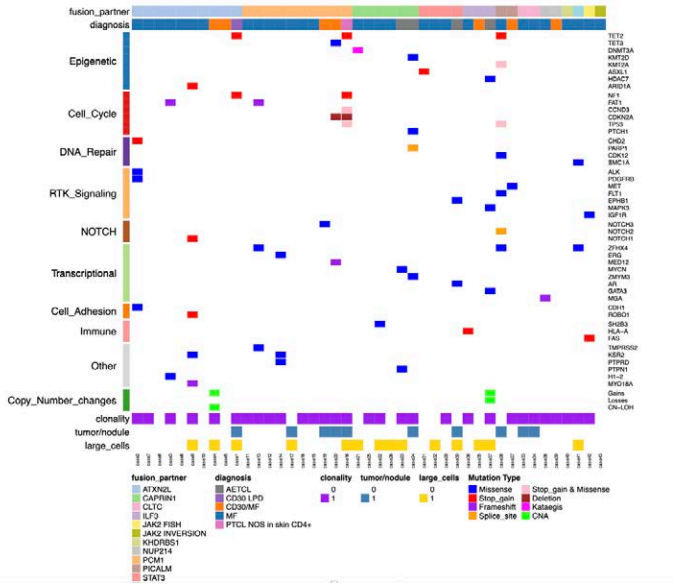
Introduction: Cutaneous T-cell lymphomas (CTCL) possess complex mutational landscapes where the role of gene is not yet well defined. While JAK-family fusions are documented in specific subtypes, the frequency and clinical implications of other fusions are undefined. This study describes the molecular features and clinical courses of a cohort of CTCL patients harboring non-JAK-family fusions detected in skin lesions.

Methods, Results: We conducted a retrospective analysis of patients with CTCL harboring predicted productive non-JAK, non-TYK gene fusions. Fusions were detected using an RNA-based anchored multiplex PCR panel. When available, results were compared with a custom DNA hybridization capture-based next-generation sequencing platform. Clinical and pathologic records were reviewed by a multidisciplinary team of specialists to confirm diagnoses.

We identified 17 patients with 20 unique gene fusions, 14 of which were previously unreported. Fusions were seen across histologies, including CD30+ T-cell lymphoproliferative disorders, mycosis fungoides, and peripheral T-cell lymphoma, not otherwise specified. Recurrent fusions involved TP63 (n=3), BCL6 (n=2), and ROS1 (n=2). Eleven cases involved transcription factors and six involved kinases (NEK6, PDGFRA, GUCY2C, ERBB4, ROS1). Patients with TP63 fusions demonstrated aggressive clinical course and resistance to standard therapies. Generally, higher tumor mutational burden and the presence of TP53 or CDKN2A alterations correlated with multiple disease relapses.



Conclusion: These findings highlight the genomic complexity of CTCL and demonstrate that multiple gene fusions are detectable across various histologies. While some fusions may indicate broad genomic instability, others represent potential therapeutic vulnerabilities. Evaluation for fusions in relapsed disease may lend insight into disease biology and point towards treatment options, such as EZH or tyrosine kinase inhibitors.

Learning Objectives:

1. Identify the variety of non-JAK gene fusions present in cutaneous T-cell lymphoma and their distribution across different clinicopathologic subtypes.
2. Describe the association between TP63 gene rearrangements and aggressive clinical behavior or treatment resistance in T-cell lymphoproliferative disorders.
3. Discuss the potential for personalized treatment strategies in refractory CTCL through the detection of targetable kinase and transcription factor fusions.

4B.06 Evaluation of TRBC1-based Clonality to Quantitate Blood Involvement in Cutaneous T Cell Lymphoma

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Introduction: Flow cytometry analysis of peripheral blood is routinely utilized to quantify immunophenotypically abnormal T-cell populations and establish blood (B) stage. The recent introduction of a monoclonal antibody targeting T-cell receptor (TCR) β-chain constant region 1 (TRBC1) has been increasingly adopted in the flow cytometric analysis of T-cells.

Methods, Results: As established in Northwestern's Hematopathology Laboratory, expression of TRBC1 in either >85% or <15% of events in a given T-cell population indicates clonality. We reviewed flow cytometry results performed at the initial visit of 89 (M:F, 1.6:1) newly diagnosed CD4+ CTCL cases seen at our institution from July 2023 to December 2025. We aim to determine if TRBC1 clonality assessment is correlated to estimated clonal size of discrete, phenotypically abnormal CD4+ T cells (defined by aberrant CD3, CD4, CD5, CD7, and/or CD26 expression).

The majority of patients had CD4+ mycosis fungoides (MF)(88%, n=78), with 8 cases of Sézary syndrome (SS) (9%) and 3 cases of CD4+ CTCL not otherwise specified (NOS) (3%). This cohort was mostly indolent, with 72 Stage I patients (IA, n = 45; IB, n = 27) and 17 advanced patients (IIA, n = 1; IIB, n = 4; IIIA, n = 3; IIIB, n = 1; IVA1, n = 7; IVA2, n = 1). Disease stage significantly predicted peripheral blood clonal T-cell burden ($p<0.001$). Increased peripheral blood clonal burden independently increased the likelihood of advanced disease stage (OR 1.91, $p<0.001$). Additionally, zero-inflated negative binomial modeling illustrated a significant association between lymphadenopathy on exam and blood burden (OR 6.7, $p < 0.05$). Correlation of TRBC1 to peripheral blood burden is pending.

Conclusion: The addition of TRBC1 clonality analysis in the evaluation of peripheral blood in CTCL patients may potentially provide a highly sensitive method for identifying malignant T cell populations in MF/SS, allowing for better diagnostics and refined disease staging.

Learning Objectives:

1. Participants should be able to understand the association between atypical clonal T-cell populations in the peripheral blood and disease stage in newly diagnosed cutaneous T-cell lymphoma (CTCL).
2. Participants should be able to understand the utility of TRBC1-based methods for identifying blood involvement in CTCL staging.

4B.07 Characterization of Adult T-Cell Leukemia/Lymphoma Patients with Specific Skin Lesions in a Tertiary Dermatological Service in Brazil

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Introduction: Human T-lymphotropic virus type-1 (HTLV-1) is endemic in some countries, including Brazil. HTLV-1 causes adult T-cell leukemia-lymphoma (ATLL), with dermatological involvement occurring in 40–70% of cases. We aimed to characterize a cohort of ATLL with cutaneous involvement from a Brazilian tertiary center.

Methods, Results: Observational retrospective cohort study with ATLL patients with skin lesions followed in a tertiary hospital in São Paulo, Brazil, between 1989-2023. Data were collected at diagnosis. Kaplan–Meier survival curves were analyzed with log-rank test, univariate and multivariate analyses were performed with Cox proportional hazards model.

Forty-four patients were included, 24 females (54.5%), 20 males (45.5%). Median age at diagnosis was 59.4 years. Classification at diagnosis was: 16/44 (36.4%) chronic (93.7% unfavorable, 6.2% favorable), 14/44 (31.8%) acute, 10/44 (22.7%) smoldering, 4/44 (9.1%) lymphoma. 18/44 patients (40.9%) had plaques; 15/44 (34.1%) nodules/tumors; 11/44 (25.0%) papules; 10/44 (22.7%) erythroderma; 7/44 (15.9%) patches; 2/44 (4.5%) ichthyosis; 1/44 (2.3%) purpura. Epidermotropism/exocytosis of lymphocytes was observed in 25/40 patients (62.5%), Pautrier microabscesses in 3/41 (7.3%). 4/40 (10.0%) had subcutaneous involvement, 2/40 (5.0%) folliculotropism, 2/40 (5.0%) angiocentrism, 1/40 (2.5%) perineural involvement. 10/40

patients (25.0%) presented lichenoid pattern. 34/43 patients (79.1%) had increased lactate dehydrogenase; 20/44 (45.5%) lymphocytosis; 6/44 (13.6%) flower cells in peripheral blood; 6/41 (14.6%) hypercalcemia; 5/41 (12.2%) hypoalbuminemia. Beta-2 microglobulin was increased in all 24 cases investigated. Monoclonal T-lymphocytes were observed in the blood of 23/30 patients (76.7%) and skin of 19/25 (76.0%). 30/44 patients (68.2%) died. Median overall survival was 32.3 months. After multivariate analysis, Shimoyama classification (acute) and urea levels were associated with poorer prognoses.

Conclusion: We described a large Brazilian cohort of ATLL with cutaneous involvement. Acute subtype and elevated urea levels were independent prognostic factors. These findings contribute to better understanding of ATLL presentation in endemic regions and may guide therapeutic approaches.

Learning Objectives:

- Recognize the spectrum of clinical and histopathologic cutaneous presentations of ATLL.
- Highlight the importance of clinicopathologic, laboratory, and molecular assessment for accurate diagnosis and prognostic stratification of cutaneous ATLL.
- Identify key prognostic factors associated with poor outcomes in cutaneous ATLL.

4B.08 Baseline Macrophage States Determine Immune Reprogramming Trajectories and Clinical Response to Extracorporeal Photopheresis in Sézary Syndrome

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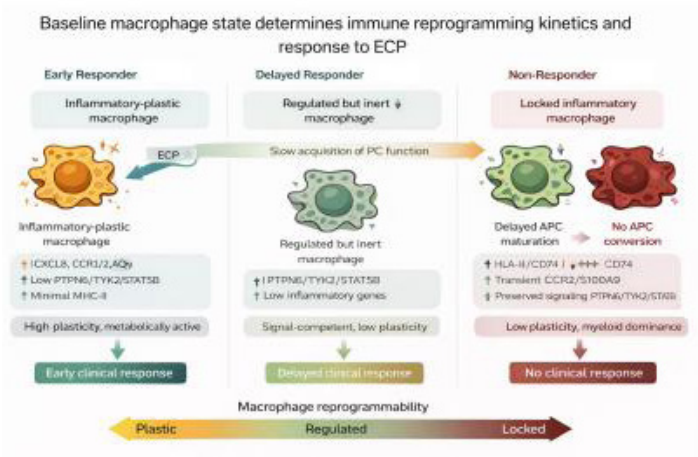
Introduction: Extracorporeal photopheresis (ECP) is a cornerstone therapy for Sézary syndrome (SS), yet clinical responses are heterogeneous and predictive biomarkers remain lacking. We hypothesized that responsiveness to ECP is determined by the baseline immune state of circulating myeloid populations rather than by treatment induced effects alone.

Methods, Results: Peripheral blood samples were obtained longitudinally from patients with Sézary syndrome enrolled in a prospective clinical trial of ECP monotherapy (NCT05157581). Samples were collected at baseline and multiple timepoints after therapy initiation (day 1, month 1, 4, and 6). Targeted single cell RNA sequencing (399 immune genes) combined with Sézary focused transcript panels (70 genes), AbSeq protein profiling (30 proteins), and paired TCR/BCR sequencing was used to characterize immune trajectories and cellular reprogramming over time. Macrophage populations demonstrated the strongest divergence between clinical outcomes. The early responders exhibited rapid transcriptional reprogramming within 24 hours of ECP characterized by induction of antigen presentation machinery (HLA DRA, DPA1, CD74) and loss of inflammatory chemokine programs (CXCL8, CCR1). In contrast, the delayed responders demonstrated preserved regulatory signaling (PTPN6, TYK2, STAT5B) with gradual induction of MHC class II pathways over several months, consistent with time dependent immune conversion. The non-responders displayed a stable inflammatory macrophage state marked by persistent S100A9, IL1B, and THBS1 expression with absent antigen presentation signatures and minimal transcriptional change following therapy. Baseline macrophage transcriptional programs therefore predicted the kinetics and magnitude of immune reprogramming following ECP.



Conclusion: These findings suggest that macrophage plasticity is a key determinant of ECP responsiveness in Sézary syndrome. Distinct baseline myeloid immune states appear to govern whether ECP triggers rapid immune conversion, delayed remodeling, or therapeutic resistance. This framework provides a basis for developing predictive biomarkers and rational combination strategies aimed at restoring antigen presentation and immune plasticity in ECP non-responders.

Learning Objectives:

- Identify distinct baseline macrophage transcriptional states associated with early, delayed, and absent response to extracorporeal photopheresis in Sézary syndrome.
- Interpret longitudinal single cell multiomic changes in myeloid populations to understand mechanisms of immune reprogramming and treatment resistance.
- Apply the concept of macrophage plasticity to guide development of predictive biomarkers and rational combination strategies for patients undergoing ECP.

4B.09 Molecular-based Reconsideration of Classification of Primary Cutaneous CD30-positive Lymphoproliferative Disorders

Suemitsu, Yamato, Kalomeris, Taylor, Geller, Shamir, Stuver, Robert, Horwitz, Steven, Ghione, Paola, Epstein-Peterson, Zachary, Vanderbilt, Chad, Zhang, Yanming, Lim, Megan S., Elenitoba-Johnson, Kojo, Pulitzer, Melissa

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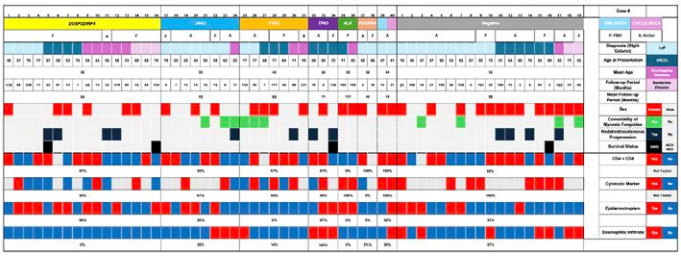
Introduction: Recently, we reported that 68% of primary cutaneous CD30+ T-cell lymphoproliferative disorders (pcCD30LPDs) in our cohort harbor gene rearrangements, a higher frequency than previously recognized, with proportions of test-negative cases roughly equal to DUSP22-rearranged and JAK-family fusion cases. Here, we compare clinicopathologic features among cases with recurrently altered genes to identify correlates of these molecular findings.

Methods, Results: An IRB-approved, large language model–guided retrospective pathology report search identified CD30LPDs with clinical ARCHER FusionPlex Pan-Heme panel testing, any positive fluorescence in situ hybridization (FISH) result, or "quad-negative" status by break-apart probes for IRF4 (DUSP22), TYK2, JAK2, and TP63, with negative ALK1 immunohistochemistry, between 2010 and 2025.

After review, 27 lymphomatoid papulosis (LyP) (46%), 17 cutaneous anaplastic large cell lymphoma (cALCL) (29%), 10 overlapping cases (LyP and cALCL) (17%), and 5 borderline cases (8%) were identified. Detailed clinical and pathologic review was performed, and descriptive analyses were conducted.

Nineteen cases (32%) were rearrangement-negative (RN). Of 40 gene-rearranged pcCD30LPDs (68%), DUSP22 rearrangements comprised 27%, JAK2/TYK2 (JAK-family) fusions 26%, and rarer fusions 11%. DUSP22 and TYK2 rearrangements were identified in both LyP and cALCL, whereas JAK2 and PDGFRA rearrangements were more often associated with LyP (7/8 and 2/2, respectively). TP63 rearrangements were restricted to cALCL (3/3). Despite dermis-limited infiltrates, JAK-family genes (JAK2 and TYK2) were the only recurrent rearrangements identified in patients with coexisting mycosis fungoides (MF) (6/15), although RN cases also showed MF (4/19). Compared with tyrosine kinase–related and "other" groups, DUSP22-rearranged cases lacked eosinophils, while TK-related cases lacked epidermal involvement. Non–JAK-family/non–DUSP22 cases more commonly showed cytotoxic marker expression.



Conclusion: Clinical and pathologic features correlate with specific recurrently altered genes in pcCD30LPD and may aid in diagnostic stratification. Although this series is small, these findings support continued efforts in molecular classification.

Learning Objectives:

1. Higher frequency and variety of gene rearranegements in primary cutaneous CD30-positive lymphoproliferative disorders.
2. Clinicopathological features associated with gene rearrangement status.
3. A new potential paradigm for classifying primary cutaneous CD30-positive lymphoproliferative disorders

SESSION 5: CUTANEOUS LYMPHOMA INTERNATIONAL CONSORTIUM: TOGETHER WE CAN

5.01 Building on CLIPI: Deeper Dive into Advanced Stage Subset

Kim, Youn H.

Stanford University School of Medicine, Palo Alto, CA, USA

Abstract not available.

5.02 Treatment Patterns in Early-Stage Mycosis Fungoides: a 10-Year Update from the PROCLIPI Study

Roccuzzo, Gabriele[1], Bashir, Abraham E.[2], Evison, Felicity[2], Kim, Youn[3], Quaglino, Pietro[1], Scarisbrick, Julia[2], Investigators, Proclipi[4]

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Introduction: The PROCLIPI trial was initiated in 2015 to prospectively characterize patients with mycosis fungoides/Sézary syndrome (MF/SS) treated at expert centers worldwide. Here, we report a 2026 update focusing on early-stage disease, following 10 years of study experience.

Methods, Results: In the international, multicenter, prospective observational PROCLIPI study, data from 46 expert MF/SS centers were collected. This analysis includes 797 early-stage MF patients (stages IA, IB, and IIA) with central pathology review and first-line treatment information. Patients were predominantly treated in non-USA (81%) centers, with 19% were enrolled in the USA; 64% were male, 36% were female. Mean age at diagnosis was 55 years (SD 17; median 57). Stage distribution was IA 51%, IB 42%, and IIA 7%. First-line management consisted of expectant management in 6%, skin-directed therapies (SDT) in 79%, and systemic therapies in 15%; combination therapies as first-lines were recorded in 2%. The most frequently used first-line treatments were topical steroids (43%, 70% of which of high potency class), UVB (20%), PUVA (13%), oral retinoids (7%, 66% of which acitretin and 33% bexarotene), with less frequent use of radiation therapy, methotrexate, interferon, topical chlormethine, and topical carmustine (each ~2%). Median time to next treatment (TTNT) was 7 months for expectant management, 11 months for SDT, and 9 months for systemic therapy. Best response to first-line therapy was complete response in 28%, partial response in 41%, and stable disease in 26%. At the time of data analysis, disease progression had occurred in 17% of patients, and death in 8%.

Conclusion: This represents the largest contemporary cohort of centrally reviewed early-stage MF patients, providing a 2026 update of real-world practice. Early-stage MF is characterized by marked therapeutic heterogeneity, with predominant use of skin-directed therapies and variable durability of first-line treatment durations.

Learning Objectives:

- Characterize the international PROCLIPI early-stage MF cohort, including 797 centrally reviewed patients (stages IA–IIA) from 46 expert centers, with key demographics and stage distribution.
- Summarize first-line treatment patterns and outcomes, highlighting predominant use of skin-directed therapies (79%), overall response rates (28% complete, 41% partial), and median time to next treatment (7–11 months).
- Evaluate disease course and durability of therapy, including progression (17%) and mortality (8%) over up to 10 years of prospective follow-up.

5.03 Navigating Therapeutic Complexity in Advanced-Stage MF/SS: Real-World Insights from the PROCLIPI Study

Bashir, Abraham E.[1,2], Roccuzzo, Gabriele[3], Evision, Felicity[1], Quaglino, Pietro[3], Kim, Youn H.[4], Scarisbrick, Julia J.[1,2], On behalf of PROCLIPI collaborators

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Introduction: Advanced-stage MF/SS includes skin tumors(stage IIB), erythroderma(stage III), and blood, nodal, or visceral involvement(stages IVA1–IVB). Management is challenging due to prior exposure to multiple therapies. This study explores real-world, prospectively collected treatment data from the PROCLIPI study(ClinicalTrials.gov ID:NCT02848274).

Methods, Results: All advanced-stage patients with treatment data in PROCLIPI (n=505), with 33%(n=168) IIB, 13%(n=64) IIIA, 10%(n=49)IIIB, 30%(n=148) IVA1, 11%(n=58) IVA2, and 3%(n=17) IVB at diagnosis were analysed. Time to next systemic treatment(TTNsT) was calculated from the initiation of the first-line treatment until the commencement/addition of another systemic therapy. At a median follow-up of 52 months, 72% of patients(n=365) received systemic, 26% received SDTs only, and 2% had expectant management.

The most common systemic therapies selected as first-line were extracorporeal photopheresis(ECP)(25.5%), methotrexate(20.1%), bexarotene(18.9%), accounting for over 60% of cases. Stratified by stage, interferon in IIB, methotrexate in IIIA-IIIB, ECP in IVA1-IVA2, and multi-agent chemotherapy in IVAB were most common. For all first-line systemic therapies, the median TTNsT was 5.8 months(IQR:3.7,11.2), with ECP achieving the longest median TTNsT of any therapy(7.7months,QR:4.5-17.6), followed by Mogamulizumab(7.5 months,IQR:5.6,22.9) and Oral Bexarotene(7.5months,IQR:4.9,14.2). Mogamulizumab also achieved the highest ORR of 83.3%, followed by Gemcitabine(77.8%) and single-agent chemotherapy regimes(66.7%).

Of all first-line treatments, 33.1%(n=167) were given as combination therapy with either an SDT or systemic. The most common therapeutics chosen for second-line treatment were ECP(21.2%), Oral Bexarotene(20.6%) and Interferon-alpha(17%). Whilst there was a large heterogeneity in individual combinations, ECP, Interferon-alpha, Oral Bexarotene and Methotrexate accounted for 68.3% of combination-therapy first-line treatment, with a median total treatment duration(including the addition of a second systemic agent) of >9months.

Conclusion: In advanced-stage MF/SS treatment selection varies substantially by disease stage, reflecting the absence of a uniform standard of care. The frequent use of combination therapies highlights the complexity of disease management and underscores the need for stage-adapted treatment strategies informed by real-world evidence.

Learning Objectives:

1. Describe real-world first- and second-line treatment patterns for advanced-stage mycosis fungoides/Sézary syndrome (MF/SS) across disease stages using data from the PROCLIPI study.
2. Compare the effectiveness of commonly used systemic and combination therapies in advanced-stage MF/SS based on time to next systemic treatment (TTNsT) and overall response rates (ORR).
3. Apply stage-adapted, real-world evidence to inform treatment selection and sequencing strategies for patients with advanced-stage MF/SS.

5.04 Blood Tumor Burden Refines Prognostication: Validation of PROCLIPI for Advanced Cutaneous Lymphoma in a Chinese Cohort

Chen, Zhuojing[1,5,6], Ruan, Yeping[2], Wang, Yimeng[3], Liu, Fengjie[4], Shen, Xiaoyan[2], Wang, Yang[1,5,6]

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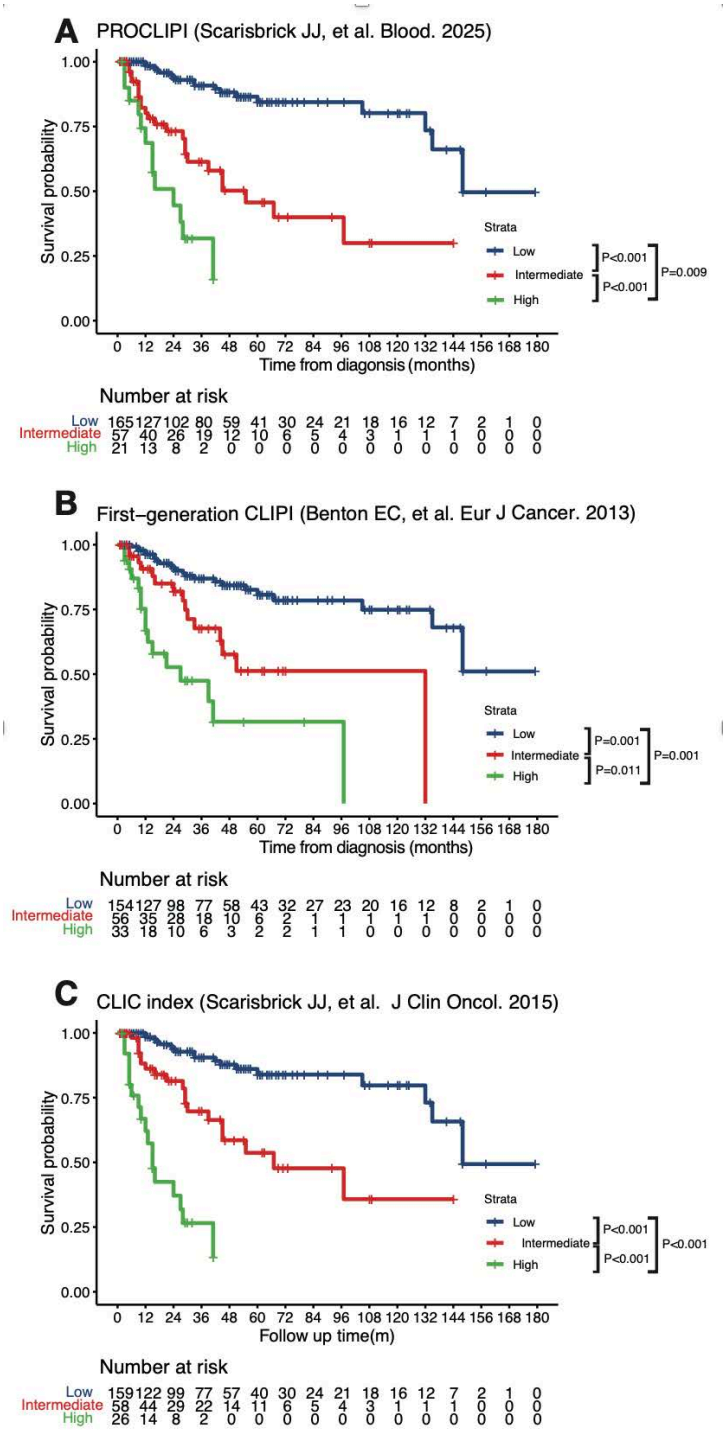
Introduction: PROCLIPI is a novel prognostic index for advanced MF/SS, but its validation in non-Western populations remains limited. This study aimed to validate PROCLIPI in a multicenter Chinese cohort and compare it with existing prognostic models.

Methods, Results: We analyzed 243 advanced MF/SS patients from the TACTICAL database (four Chinese tertiary centers). PROCLIPI risk stratification (low/intermediate/high) was applied based on age >60 years, N3 nodal involvement, elevated LDH, and large-cell transformation (LCT). Survival outcomes and prognostic model performance (discrimination via C-statistic, calibration via AIC) were evaluated and compared with first-generation CLIPI and CLIC index.

Median age at diagnosis was 52 years, with median follow-up of 28 months. PROCLIPI successfully stratified patients into low (n=165), intermediate (n=57), and high-risk (n=21) groups with 5-year OS rates of 84.4%, 45.7%, and 15.9% (all pairwise P<0.01). Multivariable analysis confirmed PROCLIPI's four factors as significant prognosticators, with B2 blood involvement also an independent predictor (HR=2.62, P=0.044). CLIC index showed marginally superior discrimination (C=0.77 vs. PROCLIPI's 0.76) and calibration (AIC=454.9 vs. PROCLIPI's 460.0), with a positive net reclassification index (3.7%).



Conclusion: PROCLIPI is valid for risk stratification in Chinese advanced MF/SS patients, confirming cross-ethnic generalizability. Incorporating blood tumor burden may enhance predictive accuracy in this population, supporting the need for ethnicity-tailored prognostic refinement.

Learning Objectives:

1. Confirm the validity and generalizability of the Prospective Cutaneous Lymphoma International Prognostic Index (PROCLIPI) in Chinese patients with advanced mycosis fungoides/Sézary syndrome (MF/SS).
2. Compare the prognostic performance of PROCLIPI with earlier models (first-generation CLIPI and CLIC index) in an East Asian cohort.
3. Identify the potential value of incorporating blood tumor burden (B2 status) into prognostic models for advanced MF/SS in Chinese populations.

5.05 How Big Is Big Enough? The Potential for Imaging-derived Quantitative Thresholds for Identifying N3 Nodal Disease in CTCL using PROCLIPI

Bashir, Abraham E.[1,5], Evision, Felicity[1], Gru, Alejandro A.[2], Battistella, Maxime[3], Kim, Youn H.[4], Scarisbrick, Julia J.[1,5], On behalf of PROCLIPI collaborators

1. University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, 2. Columbia University Irving Medical Center, New York City, NY, USA, 3. Hôpital Saint Louis, Université Paris Cité, Paris, France, 4. Stanford University School of Medicine, Palo Alto, CA, USA, 5. University of Birmingham, Birmingham, United Kingdom

Introduction: CLIPI shows N3 nodal status is associated with a significantly poorer prognosis and 5yr survival <25%. Despite this, current clinical guidelines lack standardisation in imaging techniques and LN biopsy strategies vary between centres, potentially delaying crucial identification and treatment of these patients. This study explores the potential of LN measurements from imaging as a proxy for LN biopsy in diagnosing N3 status.

Methods, Results: Analysis of all LN biopsies measurements from imaging (CT/PET), corresponding N status and patient visit data from the global PROCLIPI cohort (n=229)(ClinicalTrials.Gov ID:NCT02848274). 60%(n=140) of patients had a palpable lymph node>1.5cm on clinical assessment, of those without palpable nodes, 73%(n=66) were N3 status. Imaging identified 584 enlarged nodes(>15mm). N3 status was associated with significantly ($p<0.0001$) greater median long-axis, product diameter(PD) (long axis x short axis)and sum of product diameters(SPD), calculated by the addition of product dimension of up to six largest LNs.

These 3 nodal measures were evaluated for discrimination between N1/2 and N3 disease using a binary classification framework (N3=positive), with median-based cut-offs used to evaluate diagnostic metrics: specificity, sensitivity and Youden's J (sensitivity+specificity−1), with the threshold maximising J taken as the optimal operating point. Optimising the overall median SPD threshold from our analysis (SPD≥709mm^2) resulted in 82.5% sensitivity with 53.0% specificity - the highest observed accuracy amongst all the measures tested.

Conclusion: The study highlights N3 status was frequently present despite the absence of clinically palpable lymphadenopathy, highlighting limitations of clinical assessment alone. Imaging-derived nodal measures were significantly higher in N3 disease, with SPD demonstrating the strongest discrimination. An SPD-based diagnostic threshold optimised by Youden's J achieved a high sensitivity of 82.5%, outperforming long-axis and product diameter measures. Whilst further validation needs to be completed, our research supports SPD as a potential pragmatic, non-invasive proxy to LN biopsy to guide identification of high-risk N3 patients.

Learning Objectives:

1. Recognise the limitations of clinical lymph node palpation alone in identifying N3 nodal status in cutaneous T-cell lymphoma, and its impact on prognosis and management.
2. Evaluate imaging-derived lymph node measurements, particularly the sum of product diameters (SPD), for their ability to discriminate between N1/2 and N3 disease.
3. Apply an SPD-based diagnostic threshold from CT/PET imaging as a potential non-invasive proxy to lymph node biopsy to support earlier identification and risk stratification of high-risk N3 patients.

SESSION 6: NOVEL TARGETS FOR CTCL TREATMENT

6.01 Nivolumab with Duvelisib Leads to Repeated Immune-Mediated Toxicities in Cutaneous T-Cell Lymphoma (CTCL): Clinical Results of ETCTN Study 10347

Mehta-Shah, Neha[1], Rosenthal, Allison[2], Schatz, Jonathan H.[3], Haverkos, Bradley[5], Allen, Pamela[4], Ruan, Jia[6], Akilov, Oleg[7], Jacobsen, Eric[8], Bennani, Nora[9], Wan, Fei[1], Musiek, Amy[1], Moreno, Chaz[1], Fischer, Anne[1], Streicher, Howard[10], Said, Rabih[10], Payton, Jacqueline[1]

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Introduction: Patients with advanced stage CTCL have poor prognosis. Checkpoint inhibitors and duvelisib have response rates of 38% and 34% in CTCL respectively. Preclinical data suggests that PI3-kinase inhibition augments immunotherapy. We conducted a phase I study evaluating the safety and efficacy of nivolumab with duvelisib in stage IIB-IVB CTCL through the ETCTN.

Methods, Results: We conducted a multicenter phase I study with a 3+3 design. Patients had stage IIB-IVB CTCL, ≥1 prior systemic therapy and adequate organ function. Nivolumab 480mg IV (D1) and duvelisib (25-75mg BID) were given on a 28-day cycle until progression or intolerance. Duvelisib dosage (D1-28, BID) was escalated (DL1-25mg, DL2-50mg, DL3-75mg). Due to cumulative toxicity, a modified schedule (Schedule A) of duvelisib (D1-14, BID) was adopted (DL3a-75mg, DL2a-50mg, DL1a-25mg). Responses were evaluated after cycle 2, cycle 4 and subsequently every 3 cycles. DLTs were defined in the first 3 cycles.

Eleven patients were treated on the original schedule. Duvelisib was escalated to 75mg BID without DLT. Repeat immune-mediated AEs (4 transaminitis, 1 pneumonitis) in later cycles resulted in holding/discontinuation treatment for 6/11 patients.

Therefore, the duvelisib schedule was modified to D1-14. At DL3a, 2/2 patients developed Gr≥3 transaminitis in cycle 1. At DL2a, 2/3 patients had DLTs (Gr4 Steven's Johnsons, transaminitis). At DL1a, 2/3 patients had DLTs (Gr3 pancreatitis, Gr3 cellulitis). Therefore, toxicity exceeded the prespecified threshold.

Of the 19 patients who received treatment, 12 were evaluable for response. Overall response rate (ORR) was 4/12 (33%). Patients had a median 2 cycles. Median duration of response was 12.8 months with responses seen for 2, 9, 38 months and one remains in PR at 15 months.

Dose Level	N	Duvelisib (BID)	Best Response	Toxicities Leading to Holding/Discontinuation Treatment
Original Schedule (Duvelisib D1-28)				
1	3	25 mg	1 SD 1 PD 1 NE	- Repeated gr 2 AST/ALT
2	3	50 mg	2 SD 1 PD	- Gr 3 AST/ALT
3	5	75 mg	1 CR 1 PR 1 PD 2 NE	- Gr 4 AST/ALT - Gr 3 AST/ALT - G3 pneumonitis - Gr 5 unwitnessed arrest after sepsis
Modified Schedule A (Duvelisib D1-14)				
3a	2	75 mg	2 NE	- Grade 3 AST/ALT - Grade 4 AST/ALT
2a	3	50 mg	1 PR 2 SD	- Grade 4 AST/AST - Steven's Johnsons
1a	3	25 mg	1 PR 2 NE	- Gr 3 sepsis - Gr 3 pancreatitis

Conclusion: Duvelisib combined with nivolumab in CTCL resulted in ORR 33% similar to single-agent duvelisib or nivolumab. However, immune-mediated toxicities were dose-limiting. Studies are ongoing to understand the mechanisms of immune-mediated toxicity.

Learning Objectives:

1. Nivolumab with duvelisib was studied in a multicenter ETCTN study with ORR 33% similar to single agent duvelisib and nivolumab.
2. Nivolumab with duvelisib resulted in recurrent immune-mediated toxicities resulting in holding and discontinuation of treatment.
3. Multicenter studies in the cooperative groups are feasible in rare diseases such as CTCL.

6.02 Targeting TNFR2 with BI-1808: Immune Activation and Promising Responses in Advanced T-Cell Lymphomas

Querfeld, Christiane[2], Barta, Stefan[1], Morris, Stephen[5], Lim, Sean[3], Carneiro, Ana[4], Yachnin, Jeffrey[6], Gertsson, Susanne[7], Holmkvist, Petra[7], Karlsson, Ingrid[7], Mårtensson, Linda[7], Lindahl, Danijela[7], Piliuhin, Dmytro[7], Sundstedt, Anette[7], Teige, Ingrid[7], Wallin, Johan E.[7], Frendeus, Björn[7,8], McAllister, Andres[7]

1. University of Pennsylvania Hospital, Philadelphia, PA, USA, 2. City of Hope Comprehensive Cancer Center, Duarte, CA, USA, 3. University Hospital Southampton NHS Foundation Trust, Southampton, United

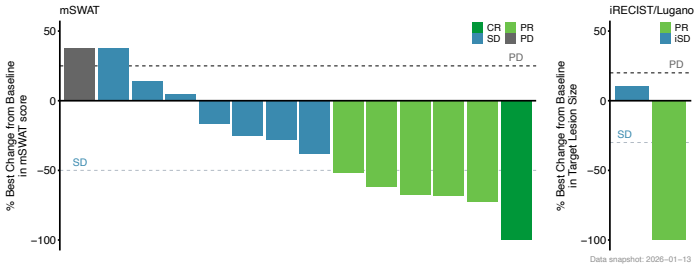
Kingdom, 4. Skåne University Hospital, Department on Hematology, Oncology and Radiation Physics, Lund, Sweden, 5. Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, 6. Karolinska Comporehensive Cancer Center, Stockholm, Sweden, 7. BioInvent International AB, Lund, Sweden, 8. Centre for Cancer Immunology, University of Southampton, Southampton, United Kingdom

Introduction: TNFR2 is implicated as a potential oncogene in T-cell lymphomas (TCL), with recurrent point mutations and gain-of-function alterations driving abnormal expression on $CD4^+CD26^-$ tumor cells. BI-1808, an IgG1 monoclonal antibody targeting TNFR2, blocks TNF-α interaction, enables FcγR-dependent regulatory T-cell depletion, and promotes intratumoral $CD8^+$ T-cell expansion. BI-1808 has demonstrated single agent activity in CTCL, PTCL, and solid tumors.

Methods, Results: We report safety and preliminary efficacy of BI-1808 monotherapy in TCL patients within a Phase 2a trial (19-BI-1808-01) as of January 13, 2026. The signal-seeking cohort enrolled 22 patients (20 CTCL, 2 PTCL) receiving BI-1808 1000 mg Q3W. Median age was 69.5 years (range 27–77); patients received a median of five cycles (range 1–24). CTCL cases included 12 MF and 8 SS advanced/metastatic, with a median of five prior systemic treatments.

Treatment-related adverse events were mainly mild or moderate; one grade 3 event was recorded. Immune-related "flare" reactions (erythema, pruritus, skin peeling) occurred early, consistent with Treg depletion and $CD8^+$ influx. Multiplex immunofluorescence of skin biopsies confirmed increased $CD8^+$ infiltration and granzyme B expression at week 5.

Among 14 evaluable CTCL patients, one SS patient achieved complete response (CR), five (4 MF, 1 SS) achieved partial response (PR), and seven had stable disease (SD). Objective response rate was 43%, and disease control rate was 93% in the evaluable CTCL population. Out of two evaluable PTCL patients (both stage IV), one achieved PR and one SD.



Conclusion: These findings indicate BI-1808 as a promising emerging safe and efficacious treatment option in advanced CTCL. Single agent treatment induces robust immune activation and promising clinical activity with an ORR of 43%. The encouraging efficacy observed in a heavily pretreated population warrants the study to proceed to dose optimization stage, which is currently recruiting.

Learning Objectives:

- Understand the biological rationale for targeting TNFR2 in T-cell lymphomas
- Evaluate the safety and preliminary efficacy findings from the Phase 2a trial of BI-1808 monotherapy
- Assess the clinical activity of BI-1808 in CTCL and PTCL

6.03 Dupilumab Use in Atopic Dermatitis When Cutaneous Lymphoma Is Suspected: Consensus Recommendations from the EORTC Cutaneous Lymphoma Task Force

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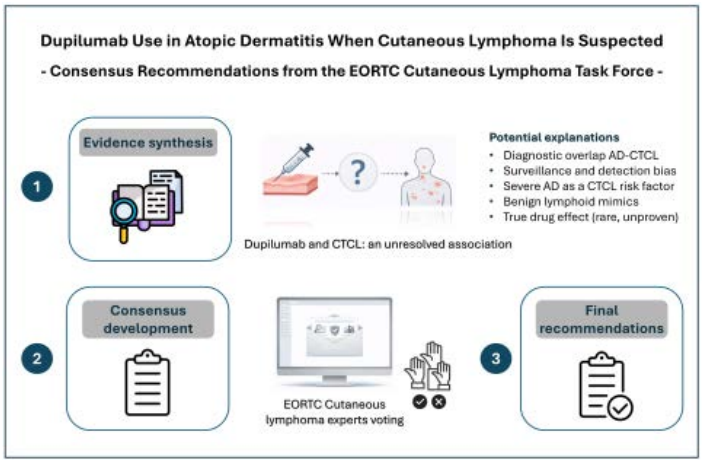
Introduction: Dupilumab is highly effective for moderate-to-severe atopic dermatitis (AD), yet increasing reports of cutaneous T-cell lymphoma (CTCL), particularly mycosis fungoides and Sézary syndrome (MF/SS), diagnosed during or after therapy, have raised concern. Although causality is unproven, real-world interpretation is complicated by AD-CTCL diagnostic overlap and by detection and surveillance bias. We aimed to provide practice-oriented recommendations for dupilumab use when CTCL is suspected.

Methods, Results: Clinical Consensus Recommendations were developed by a panel of European CTCL specialists, including members of the EORTC Cutaneous Lymphoma Task Force, using a structured questionnaire comprising 12 predefined statements informed by a focused narrative review of clinical, epidemiologic, and mechanistic evidence derived from retrospective cohorts, pharmacovigilance analyses, and case series. Levels of agreement were assessed for each statement, with high consensus achieved across the panel. Points of uncertainty were identified, discussed by the panel, and addressed within the recommendations.

The consensus emphasizes that dupilumab remains appropriate for well-defined, moderate-to-severe AD. However, dupilumab should be avoided in patients with suspected or confirmed MF/SS. In atypical or treatment-refractory AD – particularly adult-onset disease without a prior atopic history – clinicians should maintain a high index of suspicion for CTCL, with a low threshold for skin biopsy, clinicopathological correlation, and T-cell clonality assessment. During dupilumab therapy, lack of clinical response, disease worsening, or emergence of atypical features should prompt timely reassessment for CTCL rather than treatment escalation. In cases of concomitant AD and CTCL, or in palliative clinical contexts, dupilumab may be used only after multidisciplinary discussion and individualized risk-benefit evaluation; where available, alternative agents may be preferred.



Conclusion: These recommendations provide a cautious, practical approach to minimize diagnostic anchoring and delayed CTCL recognition while preserving access to dupilumab for appropriately selected AD patients. Prospective studies are needed to better define risk and refine patient selection.

Learning Objectives:

After this presentation, participants will be able to:

1. Recognize clinical scenarios in which diagnostic overlap between atopic dermatitis (AD) and cutaneous T-cell lymphoma (CTCL) warrants caution before initiating or continuing dupilumab therapy.
2. Apply consensus-based recommendations for evaluation and reassessment of patients receiving dupilumab for presumed AD who show atypical features, treatment resistance, or disease progression suggestive of CTCL. This includes skin biopsy with histopathological and immunohistochemical analysis, T-cell receptor clonality assessment, and peripheral blood immunophenotyping when indicated.
3. Integrate multidisciplinary decision-making and individualized risk–benefit assessment when managing patients with concomitant AD and CTCL or in palliative clinical contexts.

6.04 Updated Clinical Data from the Phase 1 Study of Dibotatug (DR-01), a Non-Fucosylated Anti-CD94 Antibody in Patients with Relapsed/Refractory Cytotoxic T/NK cell Lymphomas

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Introduction: Dibotatug (DR-01) is a non-fucosylated human IgG antibody targeting CD94, expressed on terminal effector CD8+T cells, γδ T cells, and NK cells leading to depletion of CD94-expressing malignant cells by antibody-dependent cellular cytotoxicity. Patients with relapsed/refractory (R/R) cytotoxic T/NK cell lymphomas (CTLs) have no effective treatment options.

Methods, Results: This Phase 1/2 open-label study (NCT05475925) is assessing dibotatug safety, pharmacokinetics (PK), pharmacodynamics, and initial efficacy and in R/R CTL patients.

As of October 2025, 81 patients with CTL (45 males) received intravenous DR-01 (0.3–10 mg/kg) in one of three induction regimens followed by monthly dosing. Median age was 53 (18–82 years) with a median of 3 (1–14) prior lines of therapy. Infusion-related reactions were the predominant treatment-related adverse events, occurring in 27 (33%) patients, primarily during initial administration, and managed effectively with standard mitigation measures.

At the selected dose (1 mg/kg; n=47), ORR was 53% (14 CR, 11 PR), with responses across histologic subtypes. The highest response rates were observed in cutaneous lymphoma histologies, with an ORR of 75% (1 CR, 5 PR) in primary cutaneous γδ T-cell lymphoma (PCγδTCL; n=8) and 80% (3 CR, 1 PR) in subcutaneous panniculitis-like T-cell lymphoma (n=5). The longest duration of response is ongoing at 22 months in a patient with PCγδTCL.

Of 44 baseline CTL study and 42 sourced samples (Samsung Medical Center, Stanford) evaluated for CD94 expression, 82 (95%) were CD94-positive by immunohistochemistry, consistent with literature showing high CD94 expression across CTL histological subtypes. Patients across a wide range of baseline CD94 expression (H-score range, 0-295) responded.

Conclusion: Dibotatug continues to demonstrate promising safety and efficacy, supporting development as a potential CTL treatment. Preliminary data suggest that patients with CTL may benefit from dibotatug regardless of baseline CD94 expression.

Learning Objectives:

- Participants will be able to identify dibotatug's (DR-01) target indication, cytotoxic T/NK cell lymphomas.
- Participants will be able to gain insights into the ongoing clinical trial, including safety and preliminary efficacy, of dibotatug (DR-01) in patients with cytotoxic T/NK cell lymphomas.

6.05 Mycosis Fungoides-Exosomes Mediate Reprogramming of Tumor-Associated Macrophages via a Novel Mechanism of CD47-Sirpα Checkpoint Interaction

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Introduction: Tumor progression of mycosis-fungoides (MF) is associated with polarization of immunosuppressive M2-macrophages within the tumor microenvironment (TME). CD47 and ICAM1 expressed on tumor cell-surface engage with SIRPα and MAC1 on macrophages, delivering "do-not-eat-me" to inhibit macrophage-mediated phagocytosis. Exosomes are small extra-cellular vesicles that mediate intercellular communication within the TME. We previously identified CD47 and ICAM1 on MF-cell line (MyLa) exosomes. This study investigated how MF-exosomes supress M1-macrophages through a novel paradigm in which exosomal-ligands engage immune-cell receptors to enforce immunosuppressive TME.

Methods, Results: Exosomes were isolated from MyLa-cells by ultracentrifugation and characterized by Nanosight and ZetaView. CD47 and ICAM1 were detected on MyLa-exosomes (Mass-spectrometry, FACS). M1-macrophages were differentiated from THP-1-monocytes and SIRPα was verified on their cell-surface (FACS). Short-exposure of M1-cells to MyLa-exosomes resulted in: exosome binding to M1-cell-membrane (spinning-disk microscopy); increased expression of M1-cytokines: IL-6 and IL-1β (qPCR); and reduced phagocytosis (phagocytic-assay); all of which were reversed by CD47/SIRPα-blockade but not by Dynasore (exosome-uptake inhibitor). This indicates that MyLa-exosomes regulate M1-macrophages through direct engagement of exosomal-CD47 to SIRPα on M1-cells. Prolonged exposure of M1-cells to MyLa-exosomes, led to complete exosome up-take, sustained increase in M1-cytokines, reduction in phagocytosis, all reversed by CD47/SIRPα-blockade, suggesting chronic-macrophage stimulation toward exhaustion and dysfunction. Sequential exposure of M1 to MyLa-exosomes shifted cytokine expression from IL-6 and IL-1β to M2-cytokines: IL-10 and TGF-β1, indicating polarization toward M2. Exosomes from plasma of MyLa-xenograft mice showed similar effects, as did exosomes from plasma of few MF-patients. RNA-seq analysis of M1-cells treated with MyLa-exosomes, confirmed CD47-SIRPα-dependent transcriptional reprogramming from M1 to M2-phenotype and M1-exhaustion.

Conclusion: MF-derived exosomes suppress antitumor M1 macrophages and promote M2 polarization through CD47–SIRPα engagement. This exosome-mediated "don't eat me" signaling provides a mechanistic link between macrophage exhaustion and impaired antitumor immunity and supports CD47 blockade as a therapeutic strategy in MF

Learning Objectives:

1. Translating exosomal CD47–SIRPα blockade into MF therapy- MF-derived exosomal CD47 functionally engages macrophage SIRPα, driving M1 exhaustion and M2-like, tumor-supportive polarization. These findings support the development of next-generation CD47-based therapeutic strategies that target both tumor cell–associated and exosome-associated CD47, with the goal of restoring macrophage antitumor activity and improving clinical outcomes in MF.
2. Exosome-mediated immune checkpoints as druggable targets- The identification of exosomal CD47–SIRPα signaling establishes exosomes as clinically relevant, cell-free immune checkpoint platforms. This provides a translational framework for systematic discovery and validation of additional exosome–immune receptor interactions that may be therapeutically targeted in CTCL and other malignancies.
3. Biomarker-guided patient selection and response monitoring- CD47-enriched plasma exosomes associate with macrophage M2-like polarization and impaired phagocytosis/antigen presentation. Integration of exosomal CD47 quantification and macrophage biomarkers into clinical studies may serve as minimally invasive markers for treatment response and disease monitoring in MF.

6.06 Preliminary Results in a First-In-Human Trial of ST-001 Nanofenretinide in Previously Treated Cutaneous T-Cell Lymphoma

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Introduction: Introduction: Patients with cutaneous T-cell lymphoma (CTCL), including mycosis fungoides (MF) and Sézary syndrome (SS), have limited durable responses to available systemic therapies. Fenretinide (4-HPR) is a synthetic retinoid active in CTCL without cross-resistance to bexarotene. ST-001 nanoFenretinide is a high-strength phospholipid nanoparticle formulation designed for intravenous use.

Methods, Results: This multicenter, phase 1, first-in-human dose-escalation study of ST-001 (NCT04234048) enrolled previously treated CTCL patients to evaluate safety, tolerability, preliminary efficacy, and pharmacology, while determining dose-limiting toxicities. ST-001, at Dose Levels 1.25–896 mg/m^2/day, was administered daily by 4-hour IV infusion for five consecutive days in 3-week cycles (maximum 8 cycles).

Eighteen patients with Stage IB–IVB CTCL (MF, n=14; SS, n=4; age range 28–82) received ST-001 after prior therapies including bexarotene, mogamulizumab, HDAC inhibitors, immunotherapy, and chemotherapeutic agents. Targeted therapeutic blood levels (~150 μM) were achieved by the higher Dose Levels. Grade 3–4 treatment-related adverse events (TRAE) occurred in five patients (28%) and included skin ulceration, acute kidney injury, hypercholesterolemia (reversible with lipid-lowering treatment), and bone/back pain. There were no treatment-related deaths; Responses included four

confirmed partial responses (PR), one unconfirmed partial response, twelve cases of stable disease (SD), and one case of progressive disease (PD), yielding an objective response rate (confirmed PR+CR) of ~28%. All responders had received prior FDA-approved systemic therapies.

Conclusion: ST-001 nanoFenretinide showed antitumor activity, including confirmed partial responses, and favorable pharmacokinetics without cytopenias, sepsis, neurologic toxicity, or hypertriglyceridemia, warranting further development to define optimized dosage and efficacy in previously treated CTCL.

Learning Objectives:

- **Understand the therapeutic rationale** for IV nanoFenretinide (ST-001) in relapsed/refractory CTCL
- **Evaluate the Phase 1 safety, pharmacokinetic, and dose-escalation data** of ST-001, with emphasis on target plasma exposure, dose-limiting toxicities, and treatment-related adverse event patterns.
- **Interpret preliminary efficacy signals** (ORR, PR/SD distribution, responder profiles) to assess clinical relevance and implications for subsequent development in previously treated CTCL populations.

6.07 Cutaneous Outcomes Associated with Nemolizumab Use in Patients with Cutaneous T-Cell Lymphoma: a Case Series

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Introduction: Nemolizumab-ilto, a subcutaneously administered monoclonal antibody inhibitor of itch-associated cytokine interleukin-31 (IL-31), is gaining interest for potential to treat refractory pruritus with cutaneous T-cell lymphoma (CTCL). Real-world data describing its use, tolerability, and clinical outcomes in this population remain limited.

Methods, Results: We performed a retrospective case series of seven patients with mycosis fungoides or Sézary syndrome (MF/SS), who received nemolizumab before or after CTCL diagnosis. We abstracted patient demographics, clinical features, timing/duration of nemolizumab therapy, pruritus response, and clinical outcomes from the medical record. Eight patients with or ultimately diagnosed with CTCL (MF/SS) received nemolizumab (Table 1). Treatment duration ranged from 1month-8 months. Five out of eight experienced initial improvements in pruritus following therapy. However, five patients developed cutaneous flares during treatment, prompting clinicopathologic evaluation. Of these, two were re-diagnosed with CTCL. One patient experienced disease progression, despite initial improvement in itch. Notably, tumor-stage disease resolved after nemolizumab discontinuation without lymphoma directed therapy. Three patients discontinued nemolizumab after one month due to lack of benefit. Lastly, one patient developed an unrelated psoriasiform eruption.

Conclusion: In this real-world case series, nemolizumab was used as adjunctive therapy for pruritus in patients with or ultimately diagnosed with CTCL with variable clinical outcomes. Despite transient improvement in itch in select patients, evidence of cutaneous flares, including unmasking CTCL when used for recalcitrant eczematous dermatitis and disease progression to tumor stage disease, should prompt caution when considering use of nemolizumab in these patient populations.

Patient age/ sex	CTCL subtype	Stage at initiation or exam prior to CTCL diagnosis	Indication	Total treatment duration	Improvement in Itch	Disease progression (maximal tumor burden)	Treatment Outcome
52 M	MF	IB	Prurigo nodularis	2.5 months	Y	Y (Stage IIB)	Discontinued due to disease progression, MF tumors and plaques regressed
75 F	MF	IA	Pruritus	1 month	N	N	Discontinued due to hypersensitivity reaction: psoriasiform and spongiotic drug eruption
89 M	-	BSA <10%, prurigo nodules	Prurigo nodularis	6-7 months	Y	New Diagnosis MF	Resolution of prurigo nodularis associated itch, discontinued to due new itchy skin eruption c/w MF (Stage IB)
77 M	MF	IB	Pruritus	4 months	Y	N	Transient improvement in pruritus and near resolution of MF; discontinued due to loss of efficacy
83 F	SS	IVA	Pruritus	1 month	N	N	Discontinued due to lack of symptomatic benefit
70 F	-	BSA 80%, erythroderma	Atopic Dermatitis	2 months	Y	New Diagnosis SS	Transient improvement of itch, Discontinued due to worsening symptoms, new diagnosis of SS
60 F	MF s/p HSCT	IIIB, erythroderma	Pruritus	8 months	Y	N	Improvement in itch coincides with addition of new lymphoma-directed therapy; Discontinued due to skin and gut GVHD in the setting of DLI
90+ M	MF	IB	Pruritus	1 month	N	N	Discontinued due to lack of improvement

Learning Objectives:

- Describe real-world patterns of nemolizumab use in patients with or subsequently diagnosed with cutaneous T-cell lymphoma, including indications, treatment duration, and clinical outcomes.
- Recognize the range of cutaneous and clinical responses observed in CTCL patients treated with nemolizumab

SESSION 7A: YOUNG INVESTIGATORS SESSION: RISK, DISPARITIES, AND DISEASE BEHAVIOR IN CUTANEOUS LYMPHOMAS

7A.01 Risk of Melanoma Skin Cancer Among Patients with Mycosis Fungoides and Sézary Syndrome. a Swedish Nationwide Population-Based Cohort Study

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Introduction: Patients with mycosis fungoides (MF) and Sézary syndrome (SS) may be more prone to skin cancer, such as melanoma. However, few studies that differ between MF and SS have employed a population-based design and assessed the correlation with skin cancer risk.

Methods, Results: This retrospective, nationwide, registry-based cohort study aimed to assess whether patients with MF and SS are at increased risk of developing cutaneous melanoma. We included all patients diagnosed with MF and SS between 1993 and 2020, using Swedish healthcare registers. Age- and sex-matched controls were selected for each patient from the general Swedish population.

Among 381 patients with MF and 33 with SS, 10 (6 males and 4 females) developed cutaneous melanoma in MF, and one female developed invasive melanoma in SS. The majority, 7 patients, had in situ melanoma, while invasive melanoma occurred in 3 patients with MF. In patients with MF, the time to melanoma ranged from 0.58 to 14.55 years, and in SS, 2.59 years. The mean age at diagnosis for MF and SS patients was 65.6 years (range 26-94) and 71.3 years (range 37-94). In the MF control group of 871,347 individuals, 10,691 cases of melanoma were identified, whereas in the SS control group of 375,144 individuals, 4,320 cases of melanoma were identified.

The hazard ratio for melanoma in patients with MF and SS compared to controls was 2.16 (95% CI: 1.16–4.02) and 3.72 (95% CI:0,52-26,41), respectively. The standardized incidence ratio was 2.05 (95% CI: 1.01–3.50) for MF and 3.78 (95% CI: 0.0–14.47) for SS (Figure 1).

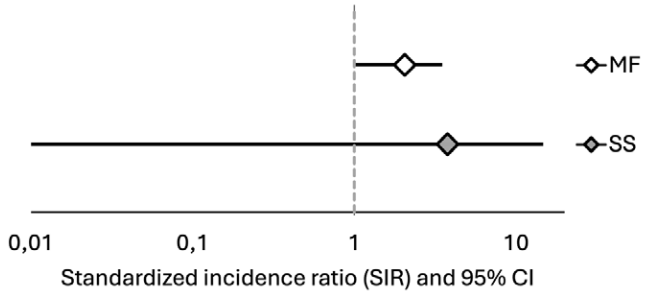

Figure 1. Standardized incidence ratio (SIRs) and 95% confidence interval (CI) for cutaneous melanoma in patients with mycosis fungoides (MF) and Sézary syndrome (SS) compared with the general population. The SS estimate is based on one observed case.

Conclusion: In this comprehensive and nationwide Swedish registry study, we showed that patients with MF and SS had an increased risk of melanoma compared to the general population. These findings underscore the importance of closely monitoring patients with MF and SS for the development of melanoma.

Learning Objectives:

1. Highlight the increased risk of cutaneous melanoma in patients with mycosis fungoides (MF) and Sézary syndrome (SS).
2. Compare differences in cutaneous melanoma risk between MF and SS using general population reference estimates.
3. Incorporate melanoma risk awareness into the clinical management of patients with MF and SS.

7A.02 Staphylococcal Hemolysins Associated with Racial Disparities and Increased Clinical Severity in Cutaneous T-Cell Lymphoma

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Introduction: *Staphylococcus aureus* is an established colonizer in Cutaneous T-Cell Lymphoma (CTCL) patients. *S. aureus* pathogenesis is mediated by secreted toxins (secretome), including hemolysins, proteases, and superantigens linked to immune evasion and malignant progression. Black CTCL patients experience more than twice the rate of invasive infections with *S. aureus*, yet the role of the *S. aureus* secretome in disparities has not been studied.

Methods, Results: Patients were consented to a prospective biobanking protocol and underwent standardized skin swabbing to generate a CTCL clinical isolate bank. Hemolysis assays were performed using rabbit blood agar to quantitate hemolysin activity. Proteomic analyses focused on samples grown in post-exponential growth stage to detect the presence of α-hemolysin, Δ-hemolysin, PSMα1, PAMα2, PAMα3, PAMα4, and V8 protease using liquid chromatography-mass spectrometry.

We evaluated an initial cohort of 33 patients, yielding 238 clinical isolates (115 from Black patients and 123 from White patients). *S. aureus* isolates exhibited significantly greater hemolytic activity than coagulase-negative staphylococci (p=0.0032), indicating an increased virulence profile. Disease was stratified by mSWAT quartiles. In the highest mSWAT quartile (mSWAT score >91), isolates from Black patients (n=66) exhibited significantly greater hemolytic activity than those from White patients (n=42) (p=0.0025). Additionally, isolates from patients with tumor-stage disease (T3) had significantly greater hemolytic activity than non-tumor stages (T1, T2, and T4) (p<0.0001). Proteomic analyses are ongoing to further characterize additional toxins in the secretome and identify virulence factors associated with severity and race.

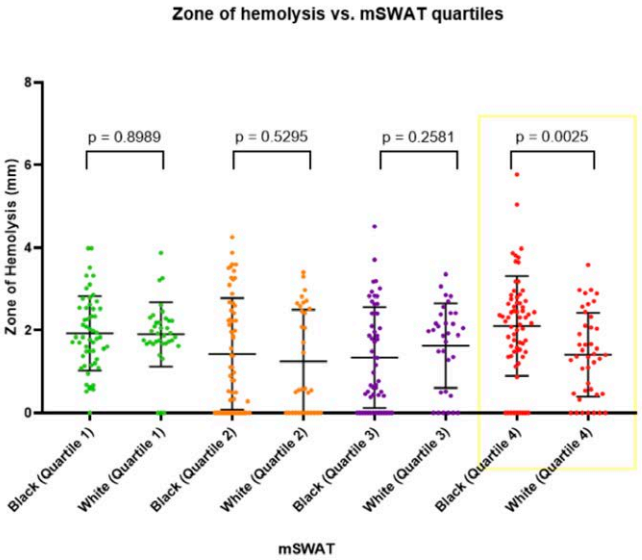

Figure 1: Comparison of hemolytic activity between Black and White *Staphylococcus aureus* isolates. Data points are individual isolates; zero values represent isolates with no detectable hemolysis. mSWAT quartiles were defined as: Q1 <9.1, Q2 9.1–39.6, Q3 39.6–91, and Q4 >91. Black Quartile 1 (n=54), White Quartile 1 (n=36), Black Quartile 2 (n=60), White Quartile 2 (n=33), Black Quartile 3 (n=54), White Quartile 3 (n=33), Black Quartile 4 (n=66), White Quartile 4 (n=42). P values calculated using a two-tailed unpaired t-test.

Conclusion: This study represents an early comparative analysis of the *S. aureus* secretome in CTCL using a racially diverse patient cohort. Integrating functional and proteomic approaches may clarify microbial contributions to CTCL progression and provide insight into biological mechanisms contributing to racial disparities in disease severity.

Learning Objectives:

1. Describe the role *of Staphylococcus aures* secretome in CTCL disease severity
2. Interpret trends in Staphylococcal hemolytic activity, and presence of other secreted virulence factors as they correlate with clinical severity in CTCL
3. Recognize how virulence factors may contribute to biological mechanisms underlying racial disparities in CTCL outcomes

7A.03 Primary Cutaneous Marginal Zone Lymphoma Developing Extracutaneous Disease: an European Organisation for Research and Treatment Cutaneous Lymphoma Tumour Group Study

Korpelshoek, L.[1,2], Willemze, Rein[1], Jansen, P.M.[2], Steeghs, E.M.P.[2], Battistella, M.[3], Beltzung, F.[4], Beylot-Barry, M.[5], Climent, F.[6], Muniesa, C.[7], Croci, G.A.[8], Kempf, Werner[9,10], Mitteldorf, C.[11], Scarisbrick, J.J.[12], Bashir, A.E.[12], Vydianath, B.[13], Wobser, M.[14], Vermeer, M.H.[1], Schrader, A.M.R.[2]

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Introduction: Primary cutaneous marginal zone lymphoma (PCMZL) is a low-grade B-cell lymphoma presenting in the skin without evidence of extracutaneous involvement at diagnosis. Despite its indolent course, there is debate whether PCMZL should be classified as a true lymphoma or rather as a lymphoproliferative disorder (LPD). An important argument in this discussion is whether extracutaneous disease (ECD) occurs, how frequently, and in which patients.

Methods, Results: In a multicentre EORTC-CTLG study, cutaneous lymphoma centres searched for patients with suspected PCMZL with progression to ECD. Eligible cases required confirmed PCMZL diagnosis with negative baseline staging. A two-day workshop was held, during which dermatologists, hematopathologists, and dermatopathologists systematically reviewed all submitted cases. For each case, clinical, histopathological, immunophenotypic and molecular data were evaluated and compared between the primary PCMZL lesion and the suspected ECD.

A total of 32 cases were submitted by seven centres. Twenty-three cases were excluded because of alternative diagnoses (n=8), prior systemic lymphoma (n=2), unrelated secondary lymphoma (n=2), positive staging (n=4), or incomplete material (n=7). Of the remaining nine cases, the relationship remained unknown in five, whereas four were considered true PCMZL progression (either by confirmed clonal relationship [n=3] or concordant morphology, immunophenotype, and clinical evolution [n=1]). Two of these four cases expressed IgM, and two expressed IgG. ECDs were marginal zone–type lymphomas, indolent in three cases and with blasts in one. No lymphoma-specific deaths occurred.

Conclusion: As demonstrated in this multicentre EORTC-CTLG study, extracutaneous progression of PCMZL is exceedingly rare but can occur. Despite progression, the clinical course of ECD cases remains indolent. Notably, ECD developed both in non-class-switched (IgM+) and class-switched (IgG+) cases. It remains a matter of debate whether rare progression to ECD can be accepted within the framework of a LPD, or whether it argues for retaining the terminology of lymphoma.

Learning Objectives:

1. Extracutaneous progression of PCMZL is exceedingly rare but can occur.
2. Accurate clinical- and histopathological review, adequate staging and assessment of clonal relationship are essential to establish an accurate diagnosis and distinguish true progression from unrelated secondary hematologic malignancies.
3. The high rate of diagnostic reclassification underscores the challenge in histopathological diagnosis of PCMZL.

7A.04 Disease Status at HSCT, Including Skin-Limited Disease, and Survival in BPDCN: a Retrospective, Multicenter Cohort Study of the EORTC, Cutaneous Lymphoma Tumour Group

Iselin, Christoph[1, 2], Roccuzzo, Gabriele[3], Dalle, Stéphane[4], Larcher, Marie-Virginie[5], Battistella, Maxime[6], Quaglino, Pietro[3], Theurich, Sebastian[7], Johanna, Tischer[7], Schmidt, Moritz[7], Pileri, Alessandro[8], Papayannidis, Cristina[9], Stadler, Rudolf[10], Meiß, Frank[11], Cozzio, Antonio[12], Vydianath, Bindu[13], Hock, Ye Lin[13], Scarisbrick, Julia[13], Guenova, Emmanuella[1, 2, 14]

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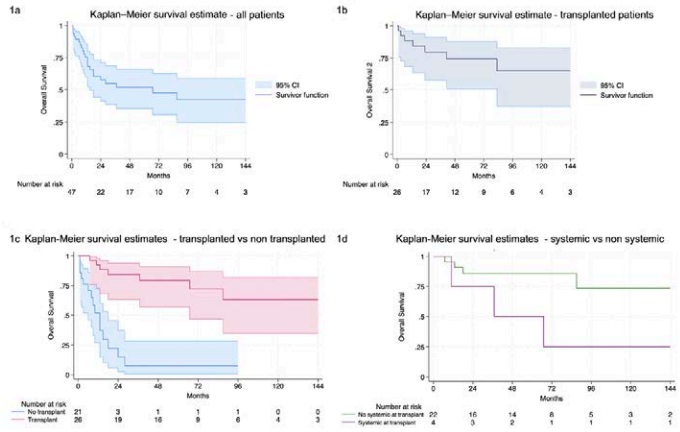
Introduction: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive hematologic malignancy that commonly involves the skin. Although hematopoietic stem cell transplantation (HSCT) is regarded as the only potentially curative treatment, the prognostic relevance of skin-limited disease remains unclear, and it is unknown whether disease status at the time of HSCT is more informative than disease distribution at diagnosis.

Methods, Results: We performed a retrospective multicentre cohort study across ten European tertiary centres affiliated with the European Organisation for Research and Treatment of Cancer (EORTC). Patients diagnosed with BPDCN from 2008 onward were included. Overall survival was analysed using Kaplan–Meier methods and Cox regression, with HSCT modelled as a time-dependent covariate to account for immortal time bias. Post-transplant survival was assessed according to disease status at HSCT.



Conclusion: In this pan-European real-world cohort, HSCT was associated with improved survival in BPDCN when analysed using a time-dependent approach. Disease status at the time of transplantation, rather than initial disease presentation, appears to provide clinically relevant prognostic information and supports the importance of achieving deep remission before HSCT whenever feasible.

Learning Objectives:

- Summarize the current treatment landscape for BPDCN, including the heterogeneity of first-line regimens and the role of HSCT as the only potentially curative option.
- Recognize the prognostic importance of disease status at time of HSCT in BPDCN, emphasizing the need to achieve remission (complete remission or skin-limited disease) before transplantation to optimize post-transplant outcomes.

7A.05 Characteristics and Outcomes of Cutaneous T-Cell Lymphoma with Gamma-Delta Phenotype: a Single-center Case Series

Lin, Stephanie K.[1], Kim, Ellen J.[1], Villasenor-Park, Jennifer[1], Myers, Caroline S.[1], Barta, Stefan K.[2], Thomas, Colin J.[2], Elghawy, Omar[2], LaRiviere, Michael[3], Plastaras, John[3], Hubbeling, Harper[3], Vittorio, Carmela C.[1], Rook, Alain H.[1], Chung, Jina[1]

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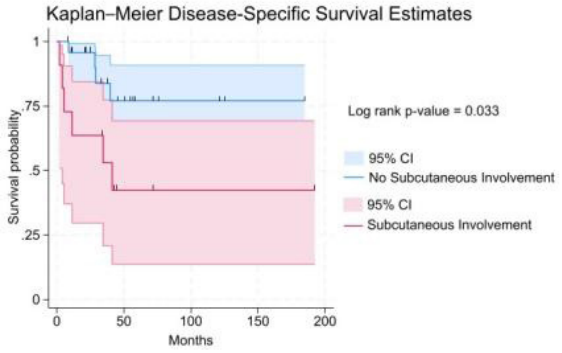
Introduction: Cutaneous T-cell lymphoma with gamma-delta (CTCL-γδ) is heterogenous in presentation, ranging from aggressive dermal/subcutaneous disease to indolent epidermotropic disease, with reported transformation rates of 30-50%.

Methods, Results: This retrospective case series identified cases of CTCL-γδ from 2006-2025 and reviewed clinical characteristics, histologic features, and outcomes. Disease-specific death was defined as death attributable to disease progression or treatment-related toxicity. Three-year disease-specific survival (DSS) and overall survival (OS) were estimated using Kaplan-Meier analysis. Comparison of survival between patients with and without subcutaneous involvement was performed using log-rank tests.

Thirty-six patients were identified, including patients initially

diagnosed with mycosis fungoides (19, 52.8%) and primary cutaneous γδ T-cell lymphoma (14, 38.9%). Eleven (30.6%) patients had subcutaneous involvement on histopathology. Fifteen (41.7%) had tumors and 9 (25.0%) had ulcers at presentation, with eventual development of tumors in a total of 24 (66.7%) and ulcers in 16 (44.4%). Extracutaneous disease was uncommon (1 blood, 2 nodal, 1 visceral). Patients were treated with a combination of topicals (35/36, 97.2%), phototherapy (11/36, 30.6%), radiation (20/36, 55.6%), oral/injection therapies such as methotrexate, interferon, bexarotene (16/36, 44.4%), infusion therapies such as chemotherapy, romidepsin, brentuximab (18/36, 50%), and hematopoietic stem cell transplantation (6/36, 16.7%). With median follow-up of 36.2 months (interquartile range 20.7-56.8), 10 disease-specific deaths occurred (6/11 with subcutaneous involvement, 4/25 without subcutaneous involvement). Overall 3-year DSS was 73.9% (95% CI 53.9-86.2%) and OS was 67.4% (95% CI 47.4-81.1%). Patients with subcutaneous involvement had significantly worse DSS compared to those without [53.0% vs. 83.9% (95% CI 20.9-77.3% vs. 57.2-94.5%); p=0.03].



Conclusion: CTCL-γδ demonstrates marked clinical heterogeneity. Subcutaneous involvement is significantly associated with worse DSS; however, disease-specific mortality also occurred in patients presenting with epidermal/dermal disease. This highlights the need for clinical follow-up and additional prognostic markers to guide management.

Learning Objectives:

- Recognize clinical and histologic heterogeneity of cutaneous T-cell lymphomas with γδ phenotype
- Identify subcutaneous involvement as an adverse prognostic factor
- Recognize disease-specific mortality can occur in patients presenting without subcutaneous involvement

7A.06 Understanding Patient Experiences and Quality of Life in Cutaneous T-Cell Lymphoma Through a Patient Education and Support Meeting

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Introduction: Cutaneous T-cell lymphoma (CTCL) is a heterogeneous non-Hodgkin lymphoma associated with significant physical and psychosocial burden. We aimed to characterize patient-reported quality of life, treatment experiences, and educational needs through a CTCL patient education and support meeting.

Methods, Results: Approximately 50 patients attended a hybrid support and education meeting, and 21 completed an anonymous survey assessing disease characteristics, treatment history, exposures, free-text responses, and Skindex quality-of-life scores. Quantitative data were analyzed descriptively, and qualitative responses were evaluated thematically.

Among respondents, 76% reported mycosis fungoides and 19% Sézary syndrome. Nine individuals (43%) were diagnosed 1-5 years ago, 5 (24%) were diagnosed 5-10 years ago, and 7 (33%) were diagnosed more than 10 years ago. The highest reported treatments were narrowband ultraviolet B (NBUVB) therapy (12), mechlorethamine gel (8) bexarotene (8), and romidepsin (5). Nine (43%) patients felt treatment made them "a lot better", eight (38%) felt treatment made them "a little better," and one (5%) felt treatment made them a little worse, and relapsing-remitting disease courses were frequently described. Skindex results demonstrated greatest burden from emotional distress (worry, frustration) and pruritus. Qualitative analysis revealed themes of uncertainty, diminished quality of life, and gratitude for care. Patients emphasized the value of clear, compassionate communication, early discussion of prognosis, and access to CTCL specialists. Identified gaps included limited education on the chronic, fluctuating disease course and delayed specialist referral.

Table 1: Patient-reported burden of skin condition during the past week (0-6 scale)

Symptom/Concern	Mean ± SD
Itching	2.73 ± 1.91
Burning or stinging	2.44 ± 2.31
Pain	2.33 ± 2.16
Skin irritation	2.40 ± 2.46
Persistence or recurrence	2.43 ± 1.72
Worry about skin condition	2.85 ± 1.83
Appearance concerns	2.25 ± 1.88
Frustration	2.33 ± 1.97
Embarrassment	1.89 ± 2.18
Annoyance	3.10 ± 1.92
Feeling depressed	2.00 ± 2.32
Reduced desire to be with people	1.67 ± 2.05
Difficulty showing affection	0.88 ± 1.96
Impact on daily activities	2.00 ± 2.10
Interference with work or enjoyable activities	1.82 ± 2.17

Conclusion: CTCL can impose substantial emotional and physical burden, with variability in treatment response, highlighting the need for individualized care. Enhanced patient education, early specialist involvement, and transparent communication may improve patient experience. Support and education meetings provide valuable insight into patient perspectives and represent an important tool for optimizing patient-centered care in CTCL.

Learning Objectives:

1. Describe key quality-of-life concerns among patients with cutaneous T-cell lymphoma (CTCL).
2. Identify patient-reported experiences with CTCL treatments.
3. Recognize opportunities to improve patient education and communication in CTCL care.

SESSION 7B: "THE GREAT TRANSFORMATION": LCT AND PREDICTING CTCL OUTCOMES

7B.01 Understanding The Molecular Triggers of Cutaneous T-Cell Lymphoma (Mycosis Fungoides) Progression

Alberti-Violetti, Silvia[1,3], Iannelli, Fabio[2], Marinucci, Laura[2], Melle, Federica[2], Spigariolo, Cristina B.[4], Venegoni, Luigia[3], Zamprogno, Marzia[1], Chiarle, Roberto[2,5,6], Pileri, Stefano A.[2], Berti, Emilio[1,7]

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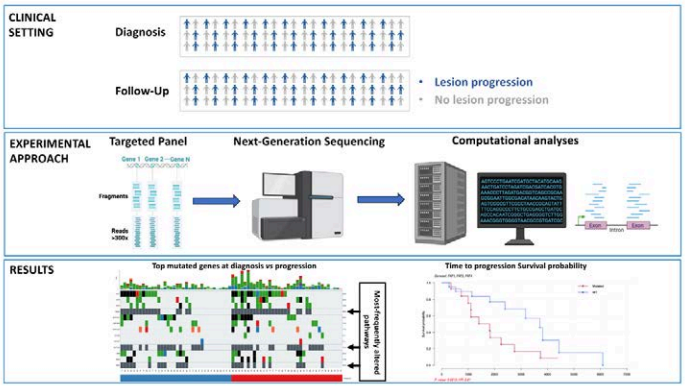
Introduction: Mycosis fungoides (MF) is a progressive form of cutaneous T-cell lymphoma where the outcome varies significantly, lasting decades or being aggressive with rapid transformation from patches and plaques to tumors or leukemia. In spite of the development of staging systems aiming to predict the clinical course, cases diagnosed in an early or advanced stage can run quite fast or very indolently, conversely to what expected.

To our knowledge studies based on the application of next generation sequencing to study MF progression are limited by a paucity of data on patient follow-up and treatment outcomes, and the genomic alterations driving disease aggressiveness remain poorly understood.

Methods, Results: Here, we performed deep coverage targeted sequencing of a panel of 113 genes known to be mutated in T-cell lymphomas on 124 MF samples from a cohort of 62 patients. Samples comprised matched diagnostic (62) and follow-up (62) skin lesion specimens. This cohort which, to our knowledge, is a first for MF in terms of size and clinical metadata, was stratified into three outcome groups: patients with (i) lesion progression accompanied by clinical upstaging, (ii) clinical upstaging without lesion progression and (iii) no clinical or lesion progression. Sequencing data were analyzed to correlate molecular alterations with clinical progression and stage dynamics.

Our study depicts a scenario with frequent mutations in genes of the Notch, TP53, and Hippo signaling pathways, the latter with recurrent mutations among patients in FAT1, FAT3, and FAT4 genes. The Hippo pathway plays a crucial role in cell proliferation, apoptosis, and response to stress, and its dysregulation is associated with poor prognosis in cancer. In particular, our analyses suggest that FAT1, FAT3 and FAT4 gene mutations are associated with a significantly worse prognosis.



Conclusion: Our results will enhance understanding of MF to stratify patients into low- and high-risk of progression and provide actionable targets.

Learning Objectives:

- Stratify patients with MF into low-risk and high-risk for progression to identify candidates for intensified therapy, including allogeneic hematopoietic stem cell transplantation.
- Predict at initial staging which patients are more likely to require active systemic therapy versus safe surveillance.
- Identify putative therapeutic targets and translate molecular findings into actionable treatment recommendations or clinical-trial options.

7B.02 Large Cell Transformation in Mycosis Fungoides/Sézary Syndrome: Contemporary Outcomes, Predictors, and Disparities Signal from the U.S. BEACON-CTCL Cohort

Qureshi, Haris[1], Ravishankar, Arjun[1], Paulino, Darina[2], Ayzman, Ann[4], Kiwan, Ahmad[1], Watkins, Marcus[4], Rosenthal, Allison[5], Mangold, Aaron[5], Beaven, Anne[6], Iyer, Swaminathan[7], Mou, Eric[8], Torres-Cabala, Carlos[7], Ghione, Paola[9], Liu, Vincent[8], Huen, Auris[7], Scribner, Jane[10], Mehta-Shah, Neha[4], Girardi, Michael[1], Foss, Francine[1], Rozati, Sima[3], Allen, Pamela[2], Sethi, Tarsheen[1]

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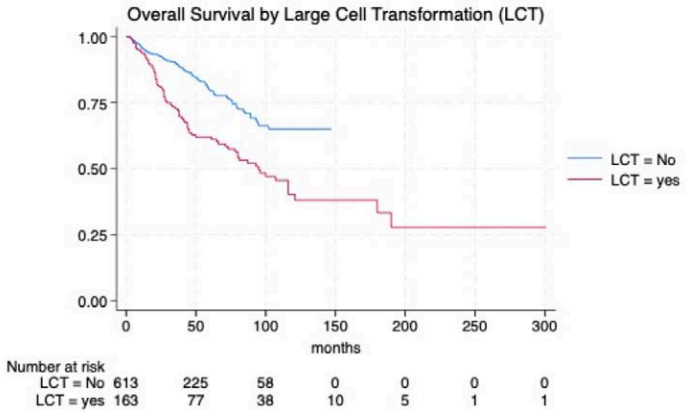
Introduction: Large cell transformation (LCT) in mycosis fungoides/Sézary syndrome (MF/SS) portends poor survival, yet specific risk factors and real-world disparities in outcomes remain incompletely defined.

Methods, Results: We conducted a retrospective study of patients diagnosed with MF/SS between 2000-2024 across 10 centers through **BEACON** (Building an Equitable and Comprehensive Oncology Network in CTCL) collaboration. Socioeconomic status was measured by Social Deprivation Index (SDI) using 2019 zip code-linked census data. LCT was defined by > 25% large cell infiltration at any site. LCT predictors were modeled via multivariable logistic regression. OS was analyzed with multivariable Cox models.

LCT was reported in 163 of 979 patients (16.6%). Multivariable logistic modeling of age, SDI, LDH, CD30 positivity, and ISCL stage at diagnosis demonstrated incremental stage was independently associated with LCT risk (OR 1.19, 95% CI 1.07-1.31;p=0.001). Median OS was 138 months (95% CI, 107–not reached; n=935). In the multivariable model adjusting for age, SDI, stage, and LDH at diagnosis, LCT was independently associated with lower OS (HR 2.97, 95% CI 1.45–6.12; p = 0.003). 82% (32/39) of LCT cases with available staining demonstrated CD30 expression ≥1%. Among 43 patients with treatment data, first-line complete response was 32.6%, partial response 48.8%, progressive disease 14%, and stable disease 4.7%; brentuximab-based regimens predominated (35%) followed by CHOP (18.6%), the latter primarily in nodal LCT.



Conclusion: In this real-world MF/SS cohort, LCT was a strong adverse factor for OS, and higher ISCL stage at diagnosis correlated with LCT risk. Brentuximab-based regimens were the most common initial therapy at transformation, with frequent post-LCT responses. These findings support risk-adapted surveillance, timely treatment escalation, and prospective evaluation of brentuximab-based therapies in high-risk patients. A cohort expansion incorporating full LCT treatment data and pathology review across the 10 centers is ongoing.

Learning Objectives:

- Identify predictors of large cell transformation (LCT) in MF/SS
- Assess the prognostic impact of LCT on overall survival (OS)
- Describe contemporary real-world treatment patterns and response outcomes after LCT

7B.03 International Study of Mycosis Fungoides with Large-Cell Transformation Confirms Poor Outcome and Reveals Heterogeneity in Presentation, Treatment and Prognosis

Campbell, Belinda A.[1,2], Passby, Lauren[3], Johnstone, Philippa[1,2], Roccuzzo, Gabriele[4], Bashir, Abraham E.[3], Quaglino, Pietro[4], Prince, H. Miles[1,2], Scarisbrick, Julia J.[3]

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Introduction: Large-cell transformation (LCT) of mycosis fungoides/ Sézary syndrome (MF/SS) is uncommon. Although not recognised in current staging, the new prognostic index for advanced MF/SS, 'CLIPI', recognises LCT as an adverse factor.(1) LCT is typically lacking from clinical guidelines, and only recently introduced into NCCN pathways(2).

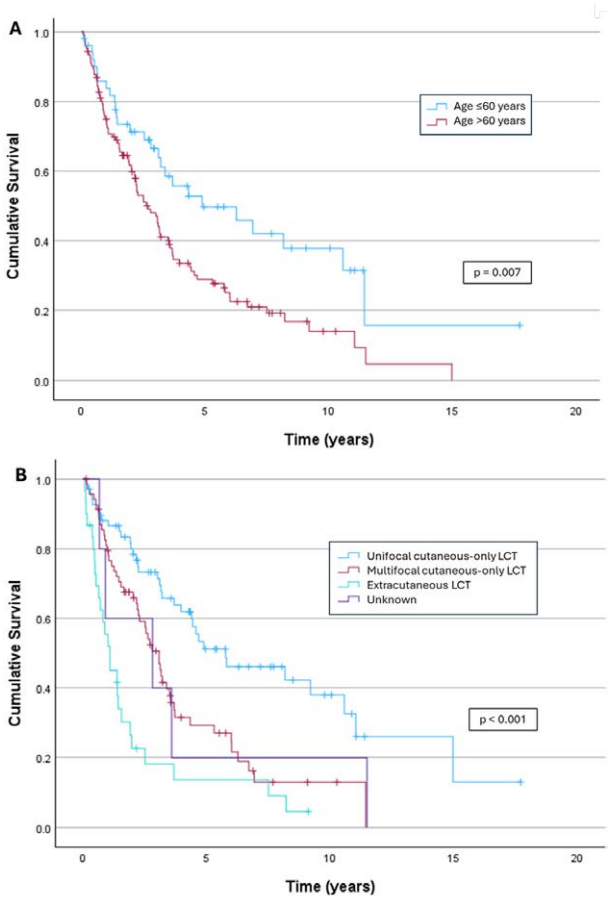
Methods, Results: Strict eligibility criteria required clinico-pathological diagnosis of MF/SS with biopsy-proven LCT. Data was retrospectively collected from Peter MacCallum Cancer Centre, Australia, University Hospital Birmingham, United Kingdom, and University of Turin, Italy.

173 patients were eligible. 107 (62%) were male. At diagnosis of LCT, median age was 68 years (range=21-91); 88 (51%) had early-stage MF/SS, 75 (43%) advanced-stage, 10 (6%) unknown. 56 (32%) presented with LCT at MF/SS diagnosis; of the remaining 117 (68%) patients, median time from MF/SS to LCT diagnoses was 4.02 years (range=0.17-29.87). LCT distribution was unifocal cutaneous-only in 68 (39%) patients, multifocal cutaneous-only in 70 (40%), extra-cutaneous in 30 (17%), and 5 (3%) unknown. 93 (54%) had cutaneous LCT tumours. 109 (63%) had CD30 expression >10%. Median follow-up was 7.17 years (range=0.06-17.70).

After LCT diagnosis, 11 different therapeutic groups were used first-line; radiotherapy being most frequent (25%). Median number of systemic treatment lines was 2 (range=0-12). 6 (3%) patients underwent allograft.

Median overall survival (OS) was 3.11 years (95%CI:2.45-3.78). 2-, 5-, 10-year OS were 64.5%, 34.9%, 21.1%, respectively.

On univariate analyses, age ≤60 years and unifocal cutaneous-only LCT were associated with statistically significant OS advantage.(Figure 1) Stage and LCT tumours were not predictive.



Conclusion: Clinical heterogeneity in LCT was observed. First-line treatment strategies were highly varied. Overall, prognosis was poor, however, those with unifocal cutaneous-only LCT had more

favourable outcomes. Future research is warranted to develop risk-adapted treatment algorithms.

References:

1. Scarisbrick et al. doi:10.1182/blood.2025029628.
2. NCCN. Primary Cutaneous Lymphomas Version 1.2024.

Learning Objectives:

1. There is heterogeneity in the presentation of large cell transformation (LCT) of mycosis fungoides / Sézary syndrome (MF/SS).
2. LCT is typically associated with poor prognosis; patients with unifocal cutaneous-only LCT and younger age have more favourable survival outcomes.
3. First-line treatment strategies for LCT are highly varied, with further research required to develop risk-adapted treatment algorithims for patients with LCT.

7B.04 Overall Survival in Transformed Mycosis Fungoides and Sézary Syndrome

Lohray, Rishabh[1], Jafarnia, Jordan[2], Copling, Sage[2], Feng, Lei[2], Sarnala, Sai[1], Arkatkar, Samruddhi[1], Ogundipe, Iyanuluwa[2], Huen, Auris O.[2], Malpica, Luis[2], Dabaja, Bouthaina[2], Dai, Julia[2], Gunther, Jillian[2], Hosing, Chitra[2], Miranda, Roberto[2], Srour, Samer[2], Ramdial, Jeremy[2], Vega, Francisco[2], Noorani, Mansoor[2], Ayers, Amy[2], Fang, Penny[2], Fayad, Luis[2], Pinnix, Chelsea[2], Duvic, Madeleine[2], Xu, Jie[2], Flowers, Christopher[2], Wu, Susan[2], Kim, Kunhwa[2], Cabala, Carlos[2], Iyer, Swaminathan[2], Nair, Ranjit[2]

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Introduction: Large Cell Transformation (LCT) is a rare phenomenon in Mycosis fungoides (MF) and Sézary Syndrome (SS), characterized by aggressive and rapid disease progression. This study aims to characterize overall survival in transformed MF/SS.

Methods, Results: Patients with MF/SS with LCT seen at MD Anderson between 1987 and 2023 were included. Overall survival (OS) was calculated from diagnosis of LCT and from initiation of first-line systemic therapy to death or last followup.

Four hundred and forty-five patients with a diagnosis of LCT were identified. The median OS time was 36.2 months (95% CI: 32.5-42 months). Prognostic factors of age at the diagnosis of LCT (adj HR: 1.028, 95% CI: 1.019- 1.038, $p < 0.0001$), advanced stage at LCT compared to early-stage (adj HR: 2.632, 95% CI: 1.674-4.140, $p < 0.0001$), extracutaneous involvement at LCT (adj HR: 1.351, 95% CI: 0.970-1.883, $p = 0.0754$), and CD30 negativity vs. positivity (adj HR: 1.476, 95% CI: 1.166-1.868, $p = 0.0012$) were identified in a multivariate analysis. In a multivariable Cox proportional hazards model, the hazard of death in patients treated with non-brentuximab vedotin (BV) therapy as a first line agent after LCT was 1.555 times higher compared to those who received BV as a first-line agent (95% CI: 1.002 ~ 2.414, $p = 0.0490$). Median survival for CD30-positive patients who received BV as first-line therapy was 78.81 months, as compared to CD30-negative patients, who had a median survival of 16.16 months ($p = 0.00079$).

Conclusion:

1. In the largest population of transformed MF/SS patients ever studied, we have identified first line use of brentuximab vedotin to be associated with improved overall survival.
2. BV's effect on improved overall survival may be most apparent in CD-30 positive patients.
3. Factors associated with poor outcomes in LCT include advanced stage, extracutaneous transformation, CD30-negativity and older age.

7B.05 Investigating the Utility of Baseline Imaging in Early-Stage Mycosis Fungoides: a Retrospective Analysis

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Introduction: Mycosis Fungoides (MF) accounts for nearly 50% cutaneous T-cell lymphomas (CTCL).1 Current National Comprehensive Cancer Network (NCCN) guidelines recommend a limited diagnostic workup for early-stage MF.2 Despite these recommendations, extensive baseline staging studies are frequently performed in clinical practice. We evaluated the frequency, indications, and clinical impact of baseline staging studies in patients with stage IA MF.

Methods, Results: We conducted a retrospective, single-center cohort study of 112 patients with stage IA CTCL/MF at diagnosis. Data collected included baseline imaging utilization, imaging indications and findings, subsequent diagnostic evaluation, and imaging-attributable treatment modifications. The primary outcome was change in clinical management directly attributable to baseline imaging.

Among 112 patients with stage IA CTCL/MF, 23 (20.5%) underwent baseline imaging, predominantly with CT-based modalities (78.3%). Indications included folliculotropic MF (n=5), granulomatous MF (n=1), staging (n=4), evaluation of adenopathy (n=2), self-reported B symptoms (n=1), concurrent malignancy (n=1), or undocumented reasons (n=9). Among patients who were imaged, 17 were ordered by providers at our institution, including by 14 cutaneous lymphoma specialists and 3 by non-specialists, one was ordered externally, and 5 had unknown ordering providers. Imaging findings were MF-related lymphadenopathy in 13.0% (n=3) of cases, an additional 13.0% were incidental (n=3), the overwhelming majority 74.0% (n=17) were negative. The clinical yield was low, with no imaging results directly impacting MF treatment decisions.

Conclusion: In patients with stage IA MF, baseline imaging was frequently performed, but rarely altered initial management. Most cases of upstaging occurred independently of baseline findings, suggesting these investigations may have limited predictive value for disease progression. These findings support a selective, guideline-concordant diagnostic approach in stage 1A MF, reserving extensive staging for clinically indicated scenarios.

References:

1. Ariza Gómez SA et al. An Bras Dermatol. 2024.
2. NCCN Guidelines V1.2026

Learning Objectives:

1. Evaluate the clinical utility of baseline imaging in stage IA MF
2. Recognize clinical scenarios in which baseline imaging is more commonly pursued
3. Apply evidence-based strategies to avoid unnecessary imaging in early-stage CTCL

7B.06 Central Nervous System Involvement in Mycosis Fungoides and Sézary Syndrome: Multicenter Series of 24 Cases from French Cutaneous Lymphoma Study Group

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Introduction: Central nervous system (CNS) involvement in mycosis fungoides (MF) and Sézary syndrome (SS) is rare and usually indicates a poor outcome. Our aims were to describe clinical features of MF/SS with CNS involvement, modalities of diagnosis, outcome and potentiel predictive factors for this involvement.

Methods, Results: In this multicenter study, we analyzed clinical features, stage of MF/SS at diagnosis of CNS involvement, mode of onset, treatments and outcome.

We included 17 MF; 7 SS : 60. Six MF were T3, and 8 had lymph node involvement. Transformation was present in 19 patients (80%). Time from MF/SS diagnosis to CNS involvement was highly variable (median: 36 months; 1 month- 36 years). When CNS localization was diagnosed, 9 had concomitant visceral involvement (lungs n = 5, eye, n= 2), but 5 had minimal or no residual skin or blood involvement. A shift in phenotype with CD8 +/- cytotoxic marker expression was observed in 7 of the 17 patients for whom information was available. Neurologic manifestations may be non-specific (asthenia or confusion n=8), sensory-motor deficits (n=8) or cranial nerve abnormalities (n=8) or even absent (n = 2). CNS Involvement vas meningeal (n= 14), parenchymal (n= 10) or concerned cranial nerves (n=6). Lumbar puncture -LP, was positive in 17 cases and brain MRI in 14, with possible discordant results. Histological confirmation was obtained in 2 cases with only parenchymal involvement. Median overall survival was 4 months with 3 patients alive (7 months - 7 years).

Conclusion: CNS involvement in MF/SS has a strong association with transformation but may also occur in patients without any recurrence of skin involvement. Modification of MF/SS phenotype with a cytotoxic features is also a warning sign. Thought, such involvment should be considered, in any MF/SS patient with aggressive course and / or neurological symptom even atypical, especially before aHSCT.

Learning Objectives:

- To be aware of possible CNS involvement in patients with transformed MF/SS or in case of phenotypic shift into cytotoxic CD8+ profile
- To consider screening with MRI in first line in such patients before aHSCT event they are otherwise in complete remission.

SESSION 8A: MORE THAN SKIN DEEP: PATIENT PERSPECTIVES IN CUTANEOUS LYMPHOMA

8A.01 Core Concepts to Assess Health-Related Quality of Life in Patients with Mycosis Fungoides and Sézary Syndrome in Clinical Trials: Results of two Electronic Delphi Rounds

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Introduction: There is currently no consensus on how to assess health-related quality of life (HRQOL) for patients with mycosis fungoides or Sézary syndrome (MF/SS). Instrument heterogeneity in clinical trials limits comparability and may miss important concepts. We aim to define a core, minimum essential set of HRQOL concepts to assess in clinical trials for MF/SS.

Methods, Results: We conducted a mixed-methods modified Delphi study including patients or care partners/advocates with MF/SS, and healthcare professionals (HCPs) with MF/SS expertise. All participants rated 53 candidate concepts across two electronic Delphi rounds (April – December 2025). Partial responses were analyzed, and ≥80% completion defined Round 2 eligibility and attrition analyses. Patient and HCP responses were weighted equally (1:1). Consensus was defined using modified OMERACT criteria[1]. Between-group differences were assessed using Mann-Whitney U tests with Bonferroni correction.

Round 1 included 183 participants (117 patient group, 66 HCP group). Ten concepts reached consensus for inclusion and were removed from subsequent voting (Table 1). Of 159 eligible invitees, 97 participated in Round 2 (50 patient group, 47 HCP group). Overall attrition was 39% (50% patient group, 20% HCP group). Nine additional concepts reached consensus for inclusion in Round 2 (Table 1). Four concepts reached inclusion consensus in one group but not in the combined weighted results. Differences between groups ($p<0.05$) were observed for two concepts (stigma, musculoskeletal symptoms). No concepts reached consensus for exclusion, and 33 remaining concepts were undecided.

Table 1. Health-related quality of life (HRQOL) concepts reaching consensus for inclusion in core set for mycosis fungoides and Sézary syndrome (MF/SS) across two electronic Delphi rounds. Concepts are grouped by the Delphi round in which they reached consensus for inclusion in the core set, and ordered by descending 1:1 weighted percentage. Patient group and Healthcare Professional (HCP) group percentages reflect the proportion voting to include each concept in the core set. Denominators vary by item because partial reponses were included in analysis.

Wellbeing Subdomain	HRQOL Concept	Patient Group (%)	HCP Group (%)	Weighted (%)
ROUND 1				
Physical-Function	Impact of itch on functional wellbeing	85%	98%	92%
Physical-Function	Impact of skin irritation, sensitivity, or pain	85%	89%	87%
Physical-Function	Impact of skin infections, oozing, weeping, bleeding	76%	91%	83%
Mental-Emotional	Impact of itch on emotional wellbeing	81%	83%	82%
Physical-Function	Impact on general activities of daily living	70%	88%	79%
Physical-Function	Impact of sleep disturbance or insomnia	71%	78%	75%
Physical-Function	Impact of disease involving hands and/or feet	63%	80%	72%
Physical-Function	Impact of skin cracking or fissuring	73%	68%	71%
Physical-Function	Impact of fatigue or tiredness	73%	67%	70%
Social	Impact of disease on work or ability to work	59%	81%	70%
ROUND 2				
Social	Impact on relationships or family life	79%	92%	85%
Mental-Emotional	Impact of visible changes from disease	83%	84%	84%
Time Toxicity	Impact of disease on time burden	85%	81%	83%
Mental-Emotional	Anxiety, worry, stress, or panic around disease	78%	85%	82%
Mental-Emotional	Efffect of treatment for disease on mental health	75%	78%	76%
Mental-Emotional	Feeling sad or depressed due to disease	62%	83%	72%
Social	Impact of itch on social wellbeing	62%	81%	71%
Mental-Emotional	Suicidal ideation due to disease	66%	75%	70%
Physical-Function	Impact of disease on exercise or mobility	72%	68%	70%

Conclusion: Across two Delphi rounds, stakeholders identified 19 HRQOL concepts as essential for MF/SS clinical trials. Essential concepts mainly clustered in physical-function wellbeing. Itch-related impacts were also deemed essential, and spanned multiple wellbeing subdomains, reinforcing pruritus as a key determinant of HRQOL in MF/SS. The lack of exclusion consensus supports structured deliberations to finalize the HRQOL core concept set.

References

1. *OMERACT HANDBOOK v2.1*. Accessed October 17, 2025.

Learning Objectives:

1. To achieve consensus among diverse stakeholders on a core set of health-related quality of life concepts to measure for patients with mycosis fungoides and Sézary syndrome in clinical trials.

8A.02 Improved Symptoms and Health-Related Quality of Life in Patients with Mycosis Fungoides and Sézary Syndrome Treated with Mogamulizumab in the PROSPER Study

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Introduction: Mycosis fungoides (MF) and Sézary syndrome (SS) cause a significant symptom burden and impair health-related quality of life (HRQL). In the phase 3 MAVORIC trial, mogamulizumab provided greater reductions in pruritus and HRQL improvements than vorinostat. The PROSPER study investigated the impact of mogamulizumab on a wider array of symptoms and HRQL in patients with MF/SS in real-world practice, incorporating cutaneous T-cell lymphoma (CTCL)-specific patient-reported outcome measures.

Methods, Results: Patients completed a CTCL-specific symptom diary (severity of skin itch, pain, redness, and flaking; sleep problems; difficulty regulating body temperature), an MF/SS-specific measure of HRQL (MF/SS-CTCL QoL), and the Brief Fatigue Inventory (BFI) before and during treatment.

Seventy-three patients were enrolled: 56% MF, 44% SS; 52% male; 82% white; mean (SD) age 67.2 (12.2) years; mean mogamulizumab treatment cycles 9.3 (4.2); 60, 61, and 58 patients, respectively, completed the Symptom Diary, MF/SS-CTCL QoL, and BFI at baseline. Mean scores for skin itch, flaking, and redness improved from baseline to week 48 (-2.5,-3.1, and -3.1, respectively); all changes exceeded the minimum important difference (MID) from week 4 (Table 1). Skin pain scores improved to -1.7 at week 48; changes exceeded the MID from week 12. The sleep problems score improved by ≥2 points for 4% of patients at week 4 and 30% at week 48. Temperature regulation improved by ≥2 points for 22% of patients at week 4 and 37% at week 48. Improvements in BFI scores were below the MID at all timepoints for MF/SS patients combined, but for SS patients were achieved in all scores at week 48. The MF/SS-CTCL QoL score improved from baseline to week 48 (-8.8) and exceeded the MID from week 12.

Table 1. Change from baseline in skin symptoms, sleep disturbance, difficulty with body temperature regulation, fatigue, and HRQL.

Patient-reported outcome[a]		Week 4			Week 12			Week 24			Week 48		
		All (n=50)	MF (n=30)	SS (n=20)	All (n=49)	MF (n=29)	SS (n=20)	All (n=45)	MF (n=27)	SS (n=18)	All (n=36)	MF (n=23)	SS (n=13)
Symptom diary													
Itchy skin	Scores, mean ± SD	**−1.4 ± 2.9†**	**−1.2 ± 2.9†**	**−1.7 ± 3.0†**	**−2.2 ± 3.6†**	**−1.9 ± 3.5†**	**−2.8 ± 3.9†**	**−2.3 ± 3.5†**	**−1.9 ± 3.6†**	**−2.9 ± 3.2†**	**−2.5 ± 3.4†**	**−2.0 ± 3.4†**	**−3.5 ± 3.2†**
Flaking skin		**−1.6 ± 2.6†**	**−1.5 ± 2. 7†**	**−1.6 ± 2.6†**	**−2.3 ± 3.2†**	**−2.4 ± 3.4†**	**−2.3 ± 3.0†**	**−2.8 ± 3.2†**	**−2.8 ± 3.3†**	**−2.9 ± 3.2†**	**−3.1 ± 3.5†**	**−3.0 ± 3.2†**	**−3.2 ± 4.1†**
Skin pain		−0.4 ± 3.5	−0.2 ± 3.5	−0.7 ± 3.6	**−1.8 ± 3.6†**	−1.3 ± 3.8	**−2.5 ± 3.3†**	**−2.2 ± 3.5†**	**−2.1 ± 3.8†**	**−2.4 ± 3.0†**	**−1.7 ± 4.4†**	−1.4 ± 4.6	**−2.2 ± 4.0**
Skin redness		**−1.9 ± 2.4†**	**−1.7 ± 2.5†**	**−2.1 ± 2.3†**	**−2.6 ± 3.3†**	**−2.9 ± 3.0†**	**−2.1 ± 3.8†**	**−2.6 ± 3.0†**	**−3.0 ± 2.9†**	**−2.1 ± 3.1†**	**−3.1 ± 3.5†**	**−2.7 ± 3.5†**	**−3.7 ± 3.5†**
Sleep problems	n (%) with ≥2 point improvement	2 (4)	1 (4)	1 (5)	12 (26)	5 (19)	7 (35)	9 (21)	4 (16)	5 (28)	10 (30)	5 (24)	5 (42)
Body temperature regulation		11 (22)	4 (14)	7 (37)	17 (36)	10 (37)	7 (35)	18 (41)	12 (46)	6 (33)	13 (37)	9 (41)	4 (31)
BFI scores, mean ± SD													
Total		Not completed			−0.5 ± 1.6†	−0.2 ± 1.7	−1.0 ± 1.4†	−0.3 ± 1.9	−0.2 ± 2.1	−0.7 ± 1.5	−0.9 ± 2.6†	−0.5 ± 2.7	−1.6 ± 2.3†
Fatigue interference					−0.4 ± 1.7	−0.4 ± 1.4	−0.4 ± 2.1	−0.3 ± 2.0	−0.3 ± 2.0	0.2 ± 2.1	−0.9 ± 2.3†	−0.7 ± 2.4	−1.3 ± 2.3
Worst fatigue					−0.6 ± 2.0	−0.3 ± 2.2	−1.0 ± 1.6†	−0.3 ± 2.3	−0.2 ± 2.6	−0.5 ± 1.9	−0.8 ± 2.9	−0.5 ± 3.0	−1.5 ± 2.7
MF/SS-CTCL QOL score, mean ± SD		Not completed			**−5.5 ± 8.7†**	**−5.7 ± 10.0†**	**−5.2 ± 6.4†**	**−6.7 ± 8.4†**	**−7.1 ± 9.2†**	**−5.8 ± 6.5†**	**−8.8 ± 8.9†**	**−7.8 ± 9.3†**	**−10.8 ± 7.9†**

[a]Skin symptoms measured on 0–10 NRS; sleep problems and difficulty with body temperature regulation were single items with five response options from 'never' to 'every night'/'always. BFI scored 0–10 NRS; MF/SS-CTCL QoL scores range 0–60.
n values are for the Symptom Diary and were similar for the BFI and MF/SS-CTCL QOL.
†Significant improvement from baseline (p<0.05). **Bold** values exceed the MID (itchy skin = −1.4; flaking skin = −1.5; skin pain = −1.6; skin redness = −1.4; BFI Total score = −1.2; BFI fatigue interference = −1.1; BFI Worst fatigue = −1.5; MF/SS-CTCL QOL = −5.4).

Conclusion: Mogamulizumab demonstrated rapid symptomatic improvements, as early as week 4, and in HRQL from week 12. The improvements were sustained throughout the 48-week study.

Learning Objectives:

1. To further understand changes in patient-reported CTCL symptoms, fatigue, and HRQL in patients with MF/SS following up to 48 weeks' treatment with mogamulizumab

8A.03 Using Skindex-29 and Targeted Instruments to Assess the Impact of Patient Factors on Quality-Of-Life and Diagnosis Understanding Over Time in Cutaneous Lymphomas

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Introduction: Cutaneous lymphomas (CL) are a rare heterogeneous group of non-Hodgkin lymphomas associated with symptomatic disfigurement, which substantially impairs quality of life (QoL). While the effects of CL on QoL have been previously explored, significant gaps remain in understanding how demographic and clinical factors impact patient QoL and diagnosis understanding across CL subtypes over time.

Methods, Results: This prospective study included 149 CL patients evaluated between 2023-2025, who completed a Skindex-29 questionnaire (symptoms, emotions, and functioning; 0-100 scale, higher scores representing poorer QoL), a pruritus scale rating, and an Understanding Your Diagnosis (UYD) survey during their initial visit. UYD is a three-question instrument that assesses patients' awareness of their cancer diagnosis and perceived prognosis. Follow-up UYD surveys were administered within 1 month. Multiple comparisons were adjusted within each domain and demographic or clinical category. Most patients (70%) had mycosis fungoides (MF) or Sézary syndrome (SS), with 67.3% of these patients exhibiting early-stage disease (IA – IIA). Overall QoL differed significantly by ethnicity/race ($p < 0.01$), diagnosis ($p < 0.001$), and stage of MF/SS ($p < 0.01$). Black patients reported lower overall QoL, lower emotional QoL, and higher pruritus scale ratings compared to White patients (all p-adjusted < 0.05). SS patients had lower functioning QoL, higher pruritus scale ratings, and more negative perceptions on future outcomes compared to MF and CD30+ lymphoproliferative disease patients (all p-adjusted < 0.05). Similarly, advanced stage MF/SS (IIB – IVB) patients indicated poorer outlooks than early-stage patients (p-adjusted < 0.05). Among 96 patients who completed the UYD survey at both timepoints, distribution of responses shifted significantly for questions on cancer diagnosis awareness, medical situation, and future outcome (all $p < 0.05$).

Conclusion: QoL and diagnosis understanding vary by ethnicity/race, diagnosis, and stage of MF/SS. Assessing these relationships and responses over time can inform more effective care approaches for CL patients.

Learning Objectives:

1. Comprehensive instruments like Skindex-29 and Understanding Your Diagnosis questionnaires allow assessment of how demographic and clinical characteristics may be associated with quality-of-life (QoL) and diagnosis understanding in cutaneous lymphoma patients.
2. Evaluation of patient QoL and diagnosis understanding at different timepoints highlight how outcomes change throughout the course of care.

8A.04 Patient-Reported Quality of Life Outcomes Following Extracorporeal Photopheresis for Cutaneous T-Cell Lymphoma and Graft-Versus-Host Disease

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Introduction: Extracorporeal photopheresis (ECP) is an established immunomodulatory therapy for patients with cutaneous T-cell lymphoma (CTCL) and graft-versus-host disease (GVHD). While clinical efficacy and safety are well described, there is limited real-world evidence describing patient-reported outcomes (PROs) and quality of life (QoL), particularly in populations requiring prolonged treatment. Understanding patient experience is essential in evaluating the overall benefit of ECP in chronic immune-mediated disease.

Methods, Results: A retrospective, survey-based analysis was conducted at Guy's Hospital, London, evaluating patient-reported quality of life outcomes in patients with CTCL and acute or chronic GVHD receiving ECP. A structured questionnaire assessed global quality of life, symptom burden, and treatment tolerability using Likert-style categorical responses (*very good* to *very poor*). Descriptive statistics were used to summarise responses.

Forty-six patients completed the survey. Overall, ECP was associated with favorable patient-reported outcomes, with 87% of respondents rating their quality of life as very good or good during treatment. A smaller proportion reported neutral outcomes, while few patients described poor or very poor quality of life.

Conclusion: In this real-world NHS experience, ECP was associated with favorable quality of life outcomes in patients with CTCL and GVHD. These findings support the role of ECP as a well-tolerated, patient-centered therapeutic option in chronic immune-mediated disease. This analysis demonstrates that extracorporeal photopheresis is associated with meaningful improvements in patient-reported quality of life, symptom burden, and functional status in individuals with cutaneous T-cell lymphoma and graft-versus-host disease. The favourable tolerability profile and sustained patient-perceived benefit

observed, including in patients with stable disease, highlight the importance of evaluating therapeutic success beyond conventional clinical response measures. These findings support the integration of patient-reported outcome measures into routine ECP practice and underscore the role of extracorporeal photopheresis as a patient-centred therapeutic strategy in the long-term management of chronic immune-mediated cutaneous disease.

Learning Objectives:

Evaluate patient-reported quality of life outcomes in individuals with cutaneous T-cell lymphoma and graft-versus-host disease receiving extracorporeal photopheresis.

Describe symptom-specific and functional benefits reported by patients undergoing extracorporeal photopheresis in routine clinical practice.

Recognise the role of patient-reported outcomes as complementary endpoints to clinical response when assessing treatment benefit in chronic immune-mediated cutaneous disease.

8A.05 Beyond Disease Control: Holistic Needs Assessment in Patients with Cutaneous Lymphoma in a Tertiary Skin Lymphoma Clinic

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Introduction: Cutaneous lymphomas (CLs) are chronic malignancies associated with visible skin disease and prolonged disease trajectories, resulting in substantial physical, psychological, and psychosocial burden. Holistic Needs Assessment (HNA) employs a validated patient-reported concerns checklist completed at key time points, followed by clinician review and referral-based care planning to identify and address unmet physical, emotional, practical, social, and spiritual needs.

Methods, Results: 68 patients with CLs completed HNA. Patient demographics and disease characteristics were recorded. HNA outcomes were analysed by quantifying the number of concerns per patient, categorising concerns into predefined domains (physical, emotional, practical, information/support, family/relationship, spiritual), and identifying most frequently reported concerns. 33 patients (47.1%) were male and 37 (52.8%) were females. Majority were White British (51.5%), others included Black (8.8%), Asian (4.4%), or mixed ethnicity (4.4%). Median age at HNA completion was 61 years (range=21–90). Most had cutaneous T-cell lymphoma (84.2%), and 12.8% had primary cutaneous B-cell lymphoma. At diagnosis, 79.4% had early-stage disease and 17.6% had advanced-stage disease. The median interval from diagnosis to HNA completion was 49.5 months (range=2–537 months).

Unmet needs were predominantly physical (45.7%) and emotional (22.9%), with additional practical, informational, family/relationship, and spiritual concerns. Most frequent concerns were dry, itchy or sore skin (n=43), anxiety (n=39), fatigue (n=37), sleep disturbance (n=32), low mood (n=28), and appearance-related (n=28). 89.7% of patients reported more than one concern.

Conclusion: This study demonstrates a high and multidimensional burden of unmet supportive care needs in patients with CLs. Despite a male predominance in CTCL of 2:1 over half of the surveys were from female patients. Our findings support the routine integration of HNA into CL care pathways and highlight the need for prospective studies and validation of HNA tools to optimise long-term supportive care in this population.

Learning Objectives:

1. **Describe** the multidimensional supportive care needs of patients with cutaneous lymphomas, including the most frequently reported physical and psychosocial concerns identified through Holistic Needs Assessment.
2. **Apply** Holistic Needs Assessment principles to integrate structured supportive care planning into routine cutaneous lymphoma clinical pathways.

SESSION 8B: EVOLVING PERSPECTIVES IN CUTANEOUS T-CELL LYMPHOMA: FROM TRADITIONAL HISTOPATHOLOGY TO ADVANCED DIAGNOSTIC AND BIOLOGICAL INSIGHTS

8B.01 Reduced Diversity in CTCL Intratumoral Microbiome is Associated with JAK/STAT Pathway Alterations, Non-European Ancestry, and Poor Survival

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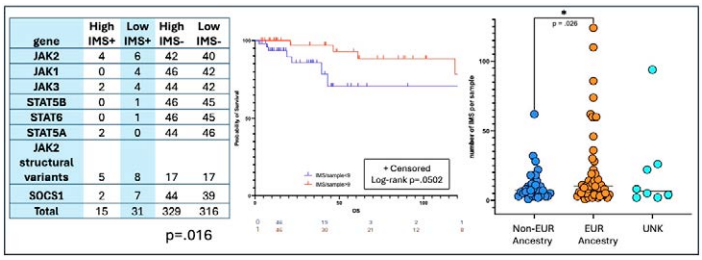
Introduction: In CTCL the tumor microenvironment (TME) is a critical component of lymphoma biology and impacts patient outcomes. Intratumoral microorganisms (IMS) are part of the TME in solid tumors and tend to localize in specific niches, influencing treatment response and outcomes. We hypothesized that IMS may impact presentation and outcomes of patients with CTCL.

Methods, Results: Targeted next-generation sequencing (NGS) was performed on CTCL biopsy samples from 93 patients (pts) followed at our institution with MSK-IMPACT and MSK-ARCHER. Microbial reads from regions that do not align with the human reference genome were analyzed. Several databases were referenced to exclude commensals and contaminants. Ancestral annotation was inferred using NGS. We compared variables across IMSs (intratumoral microbiome signatures, single-microbe-positive) present in more than 10% of the samples. ROC curve was used to estimate the AUC and best cut-off value for the IMS/sample. Median age at diagnosis in the 92 pts was 56 (20 – 90) years, 57 pts were male (52%), 55 pts had limited (IA, IB, IIA) stage CTCL 60%, 36% presented with patches, 45% with plaques, 14%) with tumors, and 5 (5%) with erythroderma. Twenty-two were of African American descent, 6 Asian, 1 Hawaiian, 53 European and 10 had mixed ancestry. The ROC curve demonstrated an AUC of 0.8 for the relation of IMS/sample and OS. Median number of IMS/sample was 13 (3-62) in African American patients and 21 (1-124) in white patients. The presence of <9 IMS per sample was associated with worse overall survival (OS), p=.052, with non-European ancestry (p=.026) and with a higher prevalence of JAK/STAT pathway alterations (mutations/fusions p=.016).



gene	High IMS+	Low IMS+	High IMS-	Low IMS-
JAK2	4	6	42	40
JAK1	0	4	46	42
JAK3	2	4	44	42
STAT5B	0	1	46	45
STAT6	0	1	46	45
STAT5A	2	0	44	46
JAK2 structural variants	5	8	17	17
SOCS1	2	7	44	39
Total	15	31	329	316

Conclusion: A low number of IMS per sample might be a sign of low intratumoral microbiome diversity and was associated with non-European ancestry, worse survival, and increased burden of JAK/STAT pathways mutations and translocations.

Learning Objectives:

- Intratumoral microbiome diversity seems to be lower in non-European pts
- Microbial signatures <9 were associated with worse overall survival and with a higher prevalence of mutations or fusions in the JAK/STAT pathway.

8B.02 Cytotoxic Hyperactivation Paired with Vascular Dysfunction and Tissue Hypoxia Mediates Lesion Self-Destruction in Lymphomatoid Papulosis

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Introduction: Cutaneous T-cell lymphomas (CTCL) comprise a heterogeneous disease spectrum ranging from indolent, self-limited lymphomatoid papulosis (LyP) to highly aggressive phenotypes. However, the underlying mechanisms of these divergent clinical behaviors are insufficiently understood.

Methods, Results: Using single-cell RNA sequencing, we profiled skin biopsies from spontaneously regressing LyP lesions of either CD4+, TCR-γδ+ or CD8+ clonal phenotypes and compared them with corresponding cases of aggressive, advanced-stage CTCL, including CD4+ or TCR-γδ+ mycosis fungoides (MF) and CD8+ aggressive epidermotropic CTCL. LyP clones exhibited a hyperactivated cytotoxic phenotype, characterized by enrichment of TNF-alpha, IL2/STAT5, interferon gamma, and complement activation pathways, irrespective of CD4+, CD8+ or TCR-γδ+ subtypes. LyP samples further demonstrated evidence of vascular dysfunction and stress (*C2CD4B, IL6, CEBPD*), corroborated by morphological signs of lymphocytic vasculitis and tissue necrosis. In contrast, malignant clones across all aggressive CTCLs lacked this inflammatory hyperactivation and instead upregulated mechanisms of tissue homeostasis, as evidenced by enriched pathways of oxidative phosphorylation, DNA repair, and glycolysis. Within the tumor microenvironment of aggressive disease, but not LyP, we also found upregulation of stress-adaptive and hypoxia-related genes such as *HIGD1A*, particularly in fibroblasts and keratinocytes.

Conclusion: Collectively, these findings suggest that LyP lesions develop a cytotoxic tissue microenvironment potentially prone to self-destruction through clonal hyperactivation and subsequent vascular dysfunction, whereas all aggressive CTCL subtypes support the formation of a robustly organized, hypoxia-resilient tumor cell niche. Taken together, this study reveals mediators associated with self-limited versus aggressive CTCL behavior that may be relevant for future immunomodulatory treatment strategies.

Learning Objectives:

1. To characterize the molecular and microenvironmental differences underlying self-limited versus aggressive cutaneous T-cell lymphomas

8B.03 Multi-Harmonic Imaging-Based Automated Recognition of Cutaneous T-Cell Lymphoma

Ghosh, Shayantani[1], Pavlova, Olesya[2], Latshaw, Alexandra[1], Kim, Doyoung[1], Iselin, Christoph[2,3], Bernard, Pauline[2], Prompsy, Pacome[2,3], Chang, Yun-Tsan[2,3], Staedler, Davide[4], Tsai, Yi-Chien[6,5], Bonacina, Luigi[1], Guenova, Emmanuella[2,3,5]

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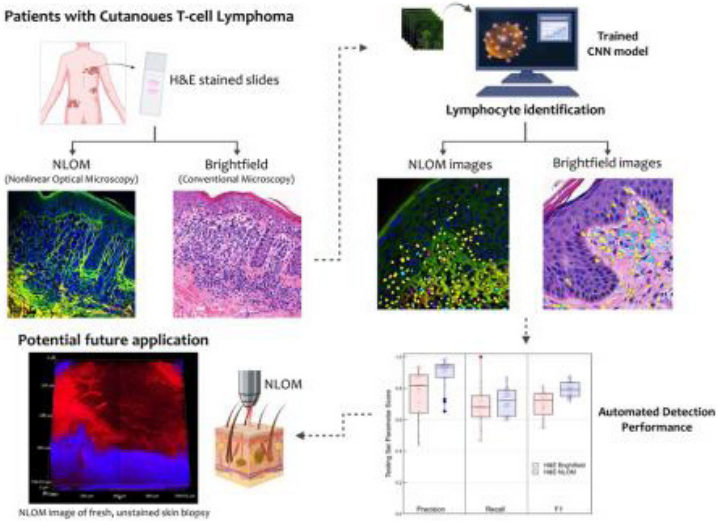
Introduction: Cutaneous T-cell lymphomas (CTCL) are a heterogeneous group of non-Hodgkin lymphomas, with mycosis fungoides (MF) being the most common type, accounting for approximately 60% of all lymphomas arising primarily in the skin. The diagnosis of MF is challenging, especially in its early stages when the number of atypical T-lymphocytes is small, and clinical and histopathologic changes are often nonspecific. This leads to significant delays of three to five years in diagnosis and treatment. Thus, novel diagnostic methods are needed to adjust the diagnostic and therapeutic strategies of CTCL. Nonlinear optical microscopy (NLOM) is promising for its sensitivity to specific tissue structures through harmonic generation and its ability to image in three dimensions.

Methods, Results: We utilise both brightfield microscopy and NLOM to analyse H&E-stained biopsy samples from MF skin lesions. Expert clinicians label the images, which are used to train a convolutional neural network (CNN) to recognise skin lymphocytes. The model is applied to independent testing datasets obtained from both imaging modalities to assess its performance in detecting characteristic features of skin T-lymphocytes. Additionally, NLOM is performed on fresh, unstained biopsy samples to highlight its potential for *in vivo* skin imaging.

NLOM successfully images epidermal and dermal structures in H&E-stained MF tissue sections with sub-cellular resolution. The trained AI model detects lymphocyte epidermotropism and dermal infiltration in the images. Moreover, NLOM imaged fresh, unstained biopsies up to 400 μm deep through the epidermis to the dermis.



Conclusion: This study demonstrates that NLOM, combined with AI, can detect lymphocyte epidermotropism and dermal infiltration in MF H&E-stained skin tissue. This approach offers dermatologists a powerful tool to improve the diagnosis and prognosis of MF-CTCL, paving the way for more timely and precise therapeutic strategies.

Learning Objectives:

1. Nonlinear optical microscopy (NLOM) can visualise epidermal and dermal cells and extracellular skin structures with sub-cellular resolution in stained and unstained samples.
2. AI-driven NLOM image analysis enables automate lymphocyte epidermotropism detection in H&E-stained MF skin sections, this expands diagnostic capabilities for skin diseases, including MF, potentially improving accuracy and outcomes.
3. NLOM can image specific tissue structures with label-free contrast, potentially enabling non-invasive diagnostics.

8B.04 Geographic and Temporal Validation of a Histopathology-Based Diagnostic Prediction Model for Risk-stratified Triage of Early-stage Mycosis Fungoides

Doeleman, Thom[1,2], Brussee, Siemen[2], Valkema, Pieter A.[2], Kempf, Werner[3], Kers, Jesper[2,4], Wynaendts, Liliane C.[5], Kerckhoffs, Kelly G.[6], de Jonge, Marthe M.[7], Nguyen, Anh H.[8], Peters, Elke E.[9], Wobser, Marion[10], Rosenwald, Andreas[11], Stadler, Rudolf[12], Jansen, Patty M.[2], Battistella, Maxime[13], Roccuzzo, Gabriele[14], Quaglino, Pietro[14], Vermeer, Maarten H.[15], Schrader, Anne M.[2]

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Introduction: The diagnosis of early-stage mycosis fungoides (eMF) is hindered by morphological overlap with benign inflammatory dermatoses (BIDs), leading to a median diagnostic delay of 36 months and substantial resource burden. We developed MIMIC (Multiple Instance-learning for Identification of Mycosis fungoides In Cutaneous biopsies), a weakly supervised diagnostic prediction model utilizing a pathology foundation model for objective, risk-stratified triage using routine H&E sections only. The goal is to expedite high-risk case identification and reduce diagnostic delay while optimizing ancillary testing.

Methods, Results: MIMIC was developed using 3,893 H&E-stained whole-slide images (WSIs) from six European centres. We implemented a dual-validation framework: (1) geographic validation across four international sites (n=383 WSIs) and a reader study with 11 (dermato-)pathologists (n=172 WSIs); and (2) a clinical utility simulation on a consecutive temporal cohort (n=550 patients, 2022–2023) to assess patient-level performance in a real-world workflow. Human-AI diagnostic behaviour and confidence were compared using a Graded Response Model. In geographic validation, MIMIC demonstrated high transportability (macro-average AUROC 0.90, n=383 WSIs) and significantly outperformed individual pathologist discrimination in the reader study (AUROC 0.81 vs. 0.74, n=172 WSIs). While pathologists frequently assigned intermediate confidence scores to borderline cases, MIMIC provided decisive MF predictions, despite some false-positive assignments among complex BIDs. Ongoing temporal validation evaluates the potential for clinical triage. Decision Curve Analysis will be used to quantify the Net Benefit across a range of risk thresholds (10–40%), assessing how the system can be calibrated to local clinical requirements to optimize immunohistochemical profiling and expert referrals.

Conclusion: Considering the inherent difficulty of eMF diagnosis, these results show promise for AI-based triage. By acting as a digital safety net at the point of initial H&E review, MIMIC could optimize specialized resources and may reduce diagnostic delay. Prospective evaluation and potential multimodal integration remain important for future clinical adoption.

Learning Objectives:

1. Understand the potential of AI models using exclusively routine H&E sections to assist in the diagnostic triage of suspected early-stage mycosis fungoides.
2. Evaluate the diagnostic performance of a risk-stratification tool compared to expert consensus across international centres.
3. Identify how H&E-based risk thresholds can be used to optimize laboratory resources while aligning with local clinical sensitivity requirements.

8B.05 Cutaneous Anaplastic Large Cell Lymphoma (ALCL): Clinical, Histopathologic, Molecular Review of 13 Cases of Primary Cutaneous ALCL & Cutaneous Involvement of Systemic ALCL

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Introduction: Anaplastic large cell lymphomas (ALCLs) are a heterogeneous group of CD30-positive mature T-cell lymphomas that may share clinical and histopathologic characteristics but are distinct in treatment recommendations, clinical course and outcomes. When manifesting in the skin, ALCL presents a diagnostic challenge for pathologists and clinicians alike.

Methods, Results: A single-center retrospective review of clinical, histopathologic and molecular data of patients with cutaneous ALCL, for whom clinical features and biopsy tissue were available for review, was performed.

Thirteen patients were identified; 9 with primary cutaneous ALCL (pcALCL) and 4 with cutaneous involvement of systemic ALCL(3 ALK-negative ALCL, 1 ALK-positive ALCL). Demographic and clinical features are summarized in Table 1. Median age was 55 years, ranging from 31 to 73 years. Ulcerated (69%) tumors and/or nodules (85%) involving the trunk (62%) and lower extremities (54%) was the most common clinical presentation. Patients with cutaneous involvement of systemic ALCL presented more commonly with greater than 10 lesions (100%, n=4), involvement of the lower extremities (100%, n=4), lymphadenopathy (100%, n=4), laboratory abnormalities (100%, n=4), and had poor outcomes, including death. Histopathologic and immunohistochemical features of pcALCL and cutaneous involvement of systemic ALCL showed overlapping findings including the presence of the "common" histologic pattern (92%), presence of Hallmark cells (100%) and comparable rates of other histopathologic and immunophenotypic features (Table 2). Multinucleated giant cells were seen more frequently in systemic ALCL (75%) than pcALCL (11%). Molecular aberrations, including *DUSP22* rearrangements, were identified in similar proportions in both groups.

Table 1. Demographic and clinical features of 13 patients with cutaneous anaplastic large cell lymphoma (ALCL)

Characteristic, n (%)	Primary cutaneous ALCL (n=9)	Systemic ALCL (n=4)	Total (n=13)	
Demographics				
Biologic Sex				
	Male	3 (33)	3 (75)	6 (46)
	Female	6 (67)	1 (25)	7 (54)
Age at diagnosis (years)				
	Median (range)	55 (43-73)	47 (31-72)	55 (31-73)
Race				
	White	7 (78)	3 (75)	10 (77)
	Black	1 (11)	1 (25)	2 (15)
	Hispanic	1 (11)	0	1 (8)
Cutaneous Manifestations				
Predominant lesion morphology				
	Nodule(s)/Tumor(s)	7 (78)	4 (100)	11 (85)
	Papule(s)	1 (11)	0	1 (8)
	Plaque(s)	1 (11)	0	1 (8)
Number of lesions				
	1	2 (22)	0	2 (15)
	2-10	3 (33)	0	3 (23)
	>10	4 (44)	4 (100)	8 (62)
Distribution of lesions †				
	Trunk	6 (67)	2 (50)	8 (62)
	Lower Extremity	3 (33)	4 (100)	7 (54)
	Upper Extremity	3 (33)	2 (50)	5 (38)
	Head/Neck	4 (44)	1 (25)	5 (38)
	Genitalia	1 (11)	2 (50)	3 (23)
Size of lesion(s)#				
	< or = 1 cm	4 (44)	4 (100)	8 (62)
	> 1 cm- 5cm	6 (67)	3 (75)	9 (69)
	>5cm -10cm	2 (22)	1 (25)	3 (23)
Ulceration				
	Present	7 (78)	2 (50)	9 (69)
	Absent	2 (22)	2 (50)	4 (31)
Healing				
	Healing with scaring	3 (33)	1 (25)	4 (31)
	UnknownΨ	5 (56)	2 (50)	7 (54)
Duration of skin lesion prior to diagnosis (months)				
	Median (range)	4 (1-144)	12 (n=1) ‡	4 (1-144) (n=10)
Symptoms				
	Pain	6 (67)	2(50)	8 (62)
	Asymptomatic	2 (22)	1(25)	3 (23)
	Unknown	1 (11)	1 (25)	2 (15)
Associated lymphadenopathy	1(11)	4 (100)	5 (38)	
Laboratory Studies				
Complete blood count abnormality at time of diagnosis				
	Any abnormality	4 (44)	4 (100)	8 (62)
	Lymphocytosis	3 (33)	3 (75)	6 (46)
	Anemia	1 (11)	2(50)	3 (23)
	Thrombocytopenia	0	1 (25)	1 (8)
Elevated serum LDH	3 (33)	2 (50)	5 (38)	
Survival				
	Alive at last follow-up	9 (100)	1 (25)	10 (77)
Follow-up duration (years)	4.3 (0.1-5.4)	3.7 (0.9-7.9)	4.3 (0.1-7.9)	

† Some patients had more than one anatomic location involved; # patients with multiple skin lesions had multiple sizes reported; Ψ Healing status unknown as lesions were treated with excision and/or radiation therapy; ‡ 3 of the four patients with systemic ALCL developed skin lesions after systemic disease diagnosis.

Abbreviations: cm, centimeters; LDH, lactate dehydrogenase; n, number,

Conclusion: The histopathologic, immunophenotypic and molecular features of pcALCL and cutaneous involvement of systemic ALCL demonstrate considerable overlap. This series highlights the necessity of clinical correlation, including obtaining clinical history and

performing a detailed physical exam and correlation with ancillary studies including lymph node biopsy findings, appropriate laboratory studies, and radiographic imaging before rendering a definitive diagnosis.

Learning Objectives:

After completion of this activity, participants will

1. Understand the most common clinical and histopathologic features of cutaneous anaplastic large cell lymphoma (ALCL).
2. Be able to identify the overlapping and distinguishing clinical and histopathologic features of primary cutaneous ALCL and cutaneous involvement of systemic ALCL.
3. Recognize the importance of correlation of clinical findings, laboratory studies, and lymph node biopsy findings in rendering a diagnosis of ALCL in the skin.

8B.06 Overlap: Mycosis Fungoides / Sézary Syndrome and Inflammatory Dermatosis, a Case Series

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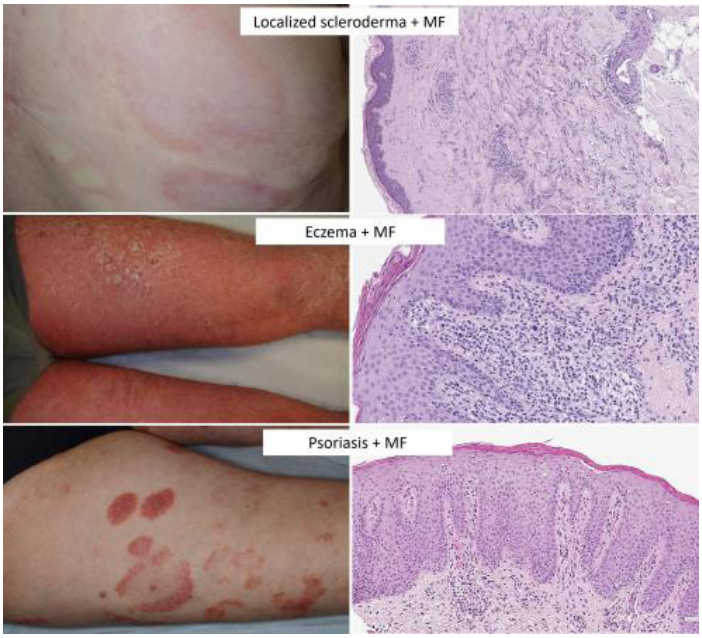
Introduction: To some extent, mycosis fungoides (MF), Sézary syndrome (SS) and inflammatory skin diseases (ISD) share their biology, as being mostly driven by skin homing T-cells, which reflects on overlapping clinic-pathologic features

Methods, Results: Series of patients with ambiguous/overlap features between ISD and MF/SS, routinely diagnosed at a single Institution. *TCRG* clonality assessed according to BIOMED-2 guidelines. Nosologic ambiguity was challenged at clinic-pathologic correlation. Definition of the ISD profile was based on the dominant ISD-like picture, comprising pattern of acanthosis, spongiosis and inflammatory background, exceeding the common histologic traits of MF/SS.

Major presenting features of 11 patients (M/F, 7/4; median age 64y): erythematous/keratotic plaques (6/11), mostly as multiple lesions in the trunk and limbs, and erythroderma (5/11), over a variable clinical course (0.5-31 yrs). Histology showed an eczematous/spongiotic profile in 7 cases, psoriasis or localized scleroderma (LS) in 2 cases each. Mayor clues to lymphoma, mostly MF (10/11), with a single psoriasis/SS, included cytologic atypia (10/11), phenotypic aberration (9/11), epidermotropism (10/11), eccrinotropism (2/11) and density of the dermal infiltrate *TCRG* proved monoclonal in all cases, with evidence of clonal identity at different sites and/or different timepoints in 10/11 cases.

Three cases (2 eczema/MF, 1 LS/MF) experienced MF progression, 1 eczema/MF case after cyclosporine administration, but followed by complete response to brentuximab; 1 eczema/MF patient died of sepsis.



Conclusion: It's debatable whether ISD-like features reflect neoplastic cell immune function, predispose to neoplasm or act as bystanders, possibly favoring MF/SS clone homing.

Correct diagnosis requires close follow-up, multidisciplinary discussion, and careful assessment of histologic pattern, lymphocyte morphology and phenotype, in an inflammatory setting. *TRCG* clonality does not prove neoplasm, but clonal persistence may support the diagnosis.

MF/SS therapies mostly target malignant cells but do not address ISD-like symptoms, which may benefit from a composite approach.

Learning Objectives:

- to discuss the challenges in diagnosing cutaneous T-cell lymphoma with inflammatory dermatosis overlap / with inflammatory changes
- to provide room for discussion on the predictive meaning of the interplay between clonal disease and immunologic function of proliferating cells

SESSION 9A: OLD TREATMENTS PERFORMING NEW TRICKS

9A.01 Long-term Outcomes After Allogeneic Stem Cell Transplantation for Cutaneous T-Cell Lymphoma

Srour, Samer A., Huen, Auris, Nieto, Yago, Dabaja, Bouthaina S., Nair, Ranjit, Ramdial, Jeremy L., Malpica Castillo, Luis E., Fayad, Luis E., Torres-Cabala, Carlos Antonio, Torres, Jennifer L., Xu, Jie, Gunther, Jillian R., Popat, Uday R., Duvic, Madeleine, Shpall, Elizabeth, Iyer, Swaminathan Padmanabhan, Hosing, Chitra

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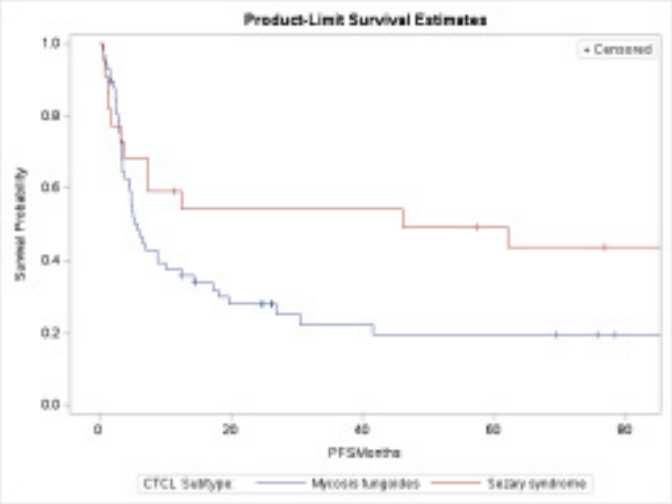
Introduction: Patients with relapsed/refractory cutaneous T-cell lymphomas (CTCLs) have limited treatment options known to confer long-term disease control. Allogeneic stem cell transplantation (Allo-

SCT) remains the only potentially curative treatment. We report on long-term experience with allo-SCT for CTCLs and explore factors predictive of improved outcomes.

Methods, Results: All consecutive patients with CTCL who underwent allogeneic SCT between July 2001 and April 2025 were included. Primary objectives were PFS and OS. Secondary objective: explore prognostic factors that impact transplant outcomes.

We analyzed 97 patients (males, 55%) with a median age of 53 years (range, 18-72). Mycosis fungoides (MF) was the most frequent subtype (n = 65), followed by Sézary syndrome (SS; n = 26). Six patients had primary cutaneous LPD (excluded from final survival analysis). Thirty-eight patients (39%) had large-cell transformation (LCT). 24 patients (27%) were in remission per TNMB staging, and 26 patients had stage IV disease (10, stage IVA; 16, stage IVB). Patients had a median of 4 prior lines of therapy. Majority had fully matched donors (n=73). 80% received fludarabine/melphalan-based reduced intensity conditioning.

With a median follow-up of 6.4 years, the 5-year PFS/OS estimates were 29%/49%. The 5-year CIR/NRM were 45%/26%. The 5-year PFS was significantly better for SS (46%) compared to MF (19%) (p=0.046). Patients with LCT had inferior 5-year PFS of 16% vs 37% for patients without LCT (p=0.0215). Transplant from fully matched siblings improved 5-year OS (58%). Forty-eight patients died during the study period, most from relapsed disease (56%), followed by GVHD (17%), infection (15%), second primary malignancy (10%) and respiratory failure (2%).



Conclusion: For patients with relapsed/refractory CTCL, Allo-SCT results in around 30% long-term disease control and potential cure. Patients with SS, those without LCT, and recipients of fully matched donors have better outcomes. Relapse remains the most frequent cause of treatment failure.

Learning Objectives:

1. Allogeneic SCT remains the only potential curative treatment for CTCL with around 30% achieving durable remissions.
2. Transplant from fully matched donors is associated with better outcomes.
3. There remains an unmet need to further improve on disease control and transplant outcomes for CTCLs.

9A.02 Exploring the Curative Potential of allo-SCT in Cutaneous T-Cell Lymphoma

Bashir, Abraham E.[1,2], Evision, Felicity[1], Kim, Youn H.[3], Scarisbrick, Julia J.[1,2], On behalf of PROCLIPI collaborators

1. University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, 2. University of Birmingham, Birmingham, United Kingdom, 3. Stanford University School of Medicine, Palo Alto, CA, USA

Introduction: Patients with advanced cutaneous lymphoma have a poor prognosis with a median survival of 1-5 years. Current guidelines recommend tailoring treatment to the disease stage. Allogeneic haematopoietic stem cell transplant (allo-SCT) is the only potentially curative therapy. Eligible patients with advanced stage disease should be considered for allo-SCT if a near-complete response is achieved. However, only a small proportion of patients proceed to allo-SCT.

Methods, Results: Data analysis of PROCLIPI(ClinicalTrials.gov ID:NCT02848274) patients who received an allo-SCT(n=47). There was a male:female ratio of 1.5(n=28:19), Median age at diagnosis was 51 years(IQR:48-56), with stage distribution of 34% early stage disease(IB=23%, IIA=11%), 66% were advanced stage(IIB=17%, IIIA=2%, IIIB=13%, IVA1=21%, IVA2=9% and IVB=4%). CLIPI risk scores distributions were high(0%), intermediate(79%), low(21%), in the patient cohort.

Median age at allo-SCT was 53 years(IQR:50-59), with stage distribution of 13% early stage(IB 4%, IIA 9%) and 87% advanced stage(IIB=19%, IIIA=11%, IIIB=11%, IVA1=19%, IVA2=23% and IVB=4%). The median time to transplant was 22 months(IQR:12-39.5). Patients received a median of 4(IQR:2-5) systemic therapies before allo-SCT. 14 different bridging therapies were selected prior to allo-SCT, of which Brentuximab(21%,n=10) was most common. Response rates following allo-SCT was 74% CR, 17% PR, 4% SD and 4% PD. Median survival was 53 months(IQR:50-59) from diagnosis, and 17 months(IQR:8-42) from allo-SCT. 40% of patients have relapsed, with a median TTNT of 4.7months(IQR:3.6-5.7). Overall mortality was 43%(n=20), with disease-specific mortality in 16 of these cases.

Conclusion: Though relapse is common, this is mostly an early-stage relapse and may be successfully managed with skin-directed therapy or donor lymphocyte infusions. Our PROCLIPI data found 57% have survived their allo-SCT, with median follow-up duration of 53 months for those who achieve complete response. This data confirms that allo-SCT may offer curative potential in some patients.

Learning Objectives:

1. Describe the clinical characteristics, treatment history, and outcomes of patients with cutaneous lymphoma undergoing allogeneic haematopoietic stem cell transplantation using PROCLIPI registry data.
2. Evaluate the efficacy and limitations of allo-SCT in advanced cutaneous lymphoma, including response rates, relapse patterns, and survival outcomes.
3. Apply evidence from real-world PROCLIPI data to identify appropriate candidates for allo-SCT and post-transplant management strategies in advanced cutaneous lymphoma.

9A.03 Interferon Alfa Lives on: Real-World Use and Safety of Pegylated Interferon Alfa-2a in Cutaneous T-Cell Lymphoma

Cruz, Christina, Cesar, Laura, Lin, Stephanie, Myers, Caroline, Thomas, Colin, Vittorio, Carmela, Chung, Jina, Villasenor-Park, Jennifer, Samimi, Sara, Rook, Alain, Barta, Stefan, Kim, Ellen J.

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Introduction: Interferon alfa is an older immunotherapy for cutaneous T-cell lymphoma (CTCL). Due to side effect concerns, its utilization has varied greatly across treatment centers. Since the discontinuation of IFNa-2b (Intron A) in 2021, pegylated interferon alfa-2a (pIFNa-2a; Pegasys) has been used as an off-label alternative. We present its use and safety in patients with CTCL at a tertiary referral center.

Methods, Results: Retrospective chart review of CTCL patients at a tertiary referral center who received pIFNa-2a for at least 3 months since October 2020. Adverse events (AEs) attributed to pIFNa-2a were graded using the CTCAE scale.

Since October 2020, 93 patients with both early and late-stage disease have been treated with pIFNa-2a. Median age was 69 (range 23-92). Median duration of pIFNa-2a treatment was 19 months (range 3-60) with a median dose of 72 mcg weekly (IQR 40-90 mcg). 26% of patients were on pIFNa-2a monotherapy, while 74% were on combination systemic therapy. AEs occurred in 74% of the 93 patients, but the majority were low-grade (53% grade 1, 30% grade 2, 13% grade 3). The most common AEs were flu-like symptoms (31% of patients) and leukopenia (31%), followed by thrombocytopenia (25%), anemia (15%), and elevated transaminases (13%). Mood changes were experienced by 10% of patients. There was 1 grade 4 event (leukopenia). All AEs were reversible with pIFNa-2a dose reduction or cessation.

68% of patients eventually discontinued pIFNa-2a. 35% of cessations were due to AEs, but the majority were for other reasons: lack of response/disease progression (17%), death unrelated to pIFNa-2a use (16%), cost (13%), self-discontinuation (8%), and complete response (5%).

Conclusion: Our large single-center series demonstrates that low-dose pIFNa-2a as monotherapy, or combination therapy, is safe and reasonably well-tolerated. 62% experienced either no or mild AEs, and severe toxicity was uncommon.

Learning Objectives:

Report pIFNa-2a dose patterns, duration of use, side effects, and discontinuation rate.

9A.04 Clinical Outcomes and Durability of Localized Radiation Therapy Versus Topical Steroids in Stage IA Mycosis Fungoides

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Introduction: Topical corticosteroids (TS) are commonly used as first-line therapy for Stage IA mycosis fungoides (MF), though complete and durable responses are variable.[1] Localized radiation therapy (RT) is highly effective for limited disease, yet comparative data evaluating durability of response between regimens are limited.[1,2] We compared clinical outcomes of RT and TS, with a focus on depth and durability of response.

Methods, Results: In this retrospective cohort study, 102 patients with biopsy-proven Stage IA MF received either low-dose RT (8 Gy; n=54) or a standardized 12-week alternating-potency TS protocol applied twice daily (n=48). Primary outcomes included complete response (CR) at 6 months and relapse-free survival (RFS). Secondary outcomes included time to next treatment (TTNT), overall response rate (ORR), and adverse events. Inverse probability weighting and multivariable regression models were used to adjust for baseline differences, including lesion morphology, number of anatomic sites, age, sex, and immunosuppression status.

RT was associated with significantly higher 6-month CR rates compared with TS (57.4% vs 21.3%, p<0.001). After adjustment, RT was associated with higher odds of achieving CR (OR 4.0, 95% CI 1.12–16.7; p=0.038). RT was also associated with significantly longer RFS, while patients treated with TS had a 3.5-fold higher risk of recurrence (HR 3.50, 95% CI 1.55–7.90; p=0.003). RT significantly prolonged TTNT (p=0.022). Adverse events were comparable between groups (13.0% vs 12.5%, p=1.0). Among lesions that failed TS therapy, 75% achieved CR following salvage RT (n=24/32).

Conclusion: Localized RT was associated with higher complete response rates and more durable disease control than TS, without increased toxicity. RT may represent an effective strategy to prolong treatment-free intervals in patients with Stage IA MF, particularly for patients who do not achieve early clearance with topical therapy.[2,3]

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Learning Objectives:

1. Describe differences in short-term response outcomes, including 6-month complete and overall response rates, between localized radiation therapy and topical corticosteroids in Stage IA mycosis fungoides.
2. Evaluate differences in response durability, relapse risk, and time to next treatment associated with radiation therapy and topical corticosteroids.
3. Compare the safety profiles of localized radiation therapy and topical corticosteroids and discuss implications for treatment sequencing and durability of disease control in early-stage mycosis fungoides.

9A.05 Systematic Review and Institutional Case Series of Intralesional Rituximab for the treatment of Primary Cutaneous B-cell Lymphoma

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Introduction: Primary cutaneous marginal zone lymphoma (PCMZL) and primary cutaneous follicle center lymphoma (PCFCL) are indolent primary cutaneous B-cell lymphomas with excellent prognoses.[1] Intralesional rituximab (ILR) has emerged as an efficacious skin-directed therapy with minimal systemic toxicity. Published data on ILR remains scant with no randomized studies highlighting its efficacy, and limited case series published, particularly in North America[2–5].

We present a systematic review and institutional case series to address efficacy, safety, dosing, and durability of response associated with ILR in indolent PCBCLs.

Methods, Results: A systematic review was conducted in accordance with PRISMA guidelines and prospectively registered in PROSPERO (CRD420251122000). MEDLINE (Ovid), Embase, and PubMed were searched for studies reporting ILR in PCMZL or PCFCL. Screening and data extraction were performed by two reviewers. Individual patient-level data were analyzed descriptively using IBM SPSS Statistics (version 31; IBM Corp., Armonk, NY, USA). In parallel, an institutional case series of six patients treated with ILR is presented.

Fifteen studies comprising 93 patients met inclusion criteria. Median age was 54.5 years (range 11-83). 62.4% were male and PCFCL accounted for 57% of cases. Lesions most commonly involved the head and neck (38.1%), extremities (36.2%), and trunk (25.7%), with 37.6% of patients having more than three lesions. Prior therapy was reported in 52.7% of patients - most commonly radiation therapy (30.3%). ILR regimens were heterogenous (median 9 injections; median cumulative dose 180 mg; median duration 6 weeks). Overall response was achieved in 89.2% of patients, including complete response in 72%; response rates were high with both weekly (85.7%) and cyclic (96.2%) dosing regimens. Recurrence occurred in 38.7% of responders. Adverse events were reported in 43% and were mild. Our institutional case series demonstrated similar efficacy and tolerability.

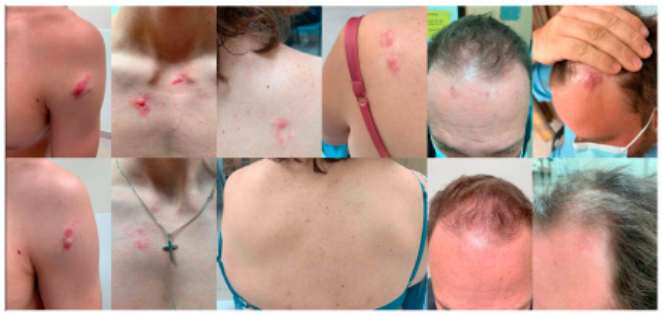

Figure 1. Clinical response to intralesional rituximab (ILR) in primary cutaneous B-cell lymphoma. Representative patients demonstrating marked reduction or complete clearance of the lesions following ILR. *Top:* prior to ILR; *Bottom:* after ILR

Conclusion: ILR is an effective and well-tolerated treatment for indolent PCBCLs, achieving high response rates with mild adverse events.

Learning Objectives:

1. To review the current literature on intralesional rituximab as a treatment for PCMZL and PCFCL.
2. To understand response rates, relapse tendencies, and adverse event profiles associated with this therapy.
3. To highlight practical considerations for incorporating intralesional rituximab into dermatologic oncology practice.

9A.06 Hands and Feet Radiation Therapy for Cutaneous T-cell lymphoma

El Alaoui, Ahmadou B., Lapen, Kaitlyn, Liao, Viviane, Gillis, Maura, Oh, Christina, Virgen, Cesar, Stuver, Robert, Ghione, Paola, Epstein-Peterson, Zachary, Horwitz, Steven, Zain, Jasmine, Johnson, William, Moskowitz, Alison, Moore, Zachary, Cederquist, Gustav, Moy, Andrea, Pulitzer, Melissa, Yahalom, Joachim, Imber, Brandon S., Geller, Shamir

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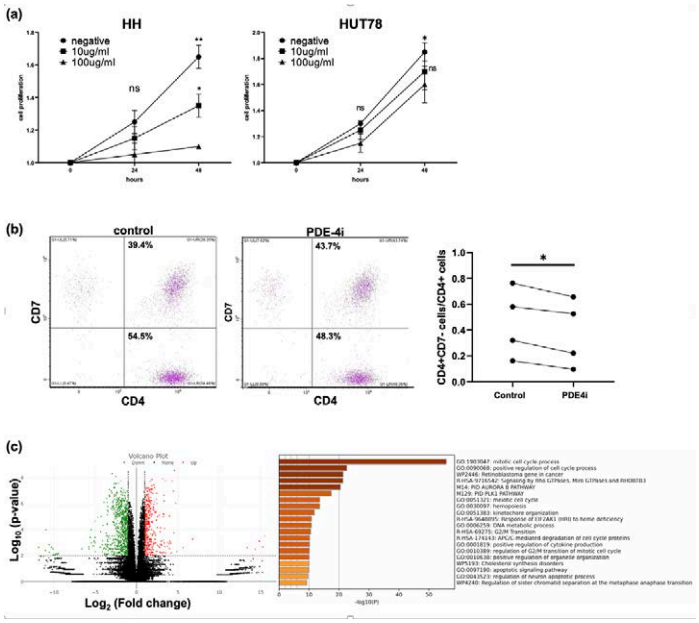
Introduction: The treatment of cutaneous T-cell lymphoma (CTCL) affecting the palmo-plantar skin presents significant challenges due to the limited penetration of skin-directed therapies, including topical treatments and phototherapy. Although radiation therapy (RT) is a cornerstone in the management of CTCL, its use for hands and feet involvement has not been studied.

Methods, Results: In this single-center retrospective study we evaluated CTCL patients who were treated with RT to hands and feet between 2012-2023. Our review encompassed the medical charts and clinical photographs to abstract demographic data, clinical characteristics and treatment parameters. Response to RT was determined by clinical document and clinical photography review.

38 patients (median age 63, range 29-89) with CTCL, mostly mycosis fungoides (MF, n=34; stages IA-IIA in 52%, IIB in 23%, III-IV 25%) received RT to hands and feet involvement by disease. We analyzed 61 radiation courses administered to feet (56%), hands (34%), and both hands and feet (10%). Total RT dose was <12Gy in 20 sessions (33%), 12-20Gy in 33 (54%) and >20Gy in 8 (13%); total dose ranged between 3-40Gy; delivered in 2-20 fractions, 1.5-4Gy per fraction. Most frequent concomitant treatments during RT were bexarotene (15%), brentuximab vedotin (8%), full body phototherapy (8%) and romidepsin (5%). Complete response was documented following 41 RT sessions (67%), partial response 14 (23%), and no response 6 (10%). Response differed by age; non-responders were older (median 74) compared to complete and partial responders (59 and 56, respectively, p=0.015). No associations were identified between response and RT dose, concomitant treatment or MF stage. Seventeen repeat RT courses were delivered to the same site, with trend toward reduced response compared to initial courses (p=0.09).



Conclusion: Palliative low dose RT to the hands and feet is highly effective for the management of palmo-plantar CTCL lesions, specifically in younger patients, and can be repeated if needed.

Learning Objectives:

1. Describe the clinical challenges of treating palmo-plantar CTCL and the rationale for using radiation therapy.
2. Summarize typical hands/feet RT practice patterns in this cohort and the observed efficacy.
3. Identify key outcome modifiers. particularly the association between older age and non-response and efficacy of repeated RT courses to hands and feet.

9A.07 The Therapeutic Potential of PDE4 Inhibitors in Mycosis Fungoides and Sézary Syndrome: A Brief In Vitro Study

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Introduction: Mycosis fungoides (MF) and Sézary syndrome (SS) are cutaneous T-cell lymphomas that often mimic inflammatory skin diseases, such as atopic dermatitis (AD)and psoriasis, leading to diagnostic challenges. Topical and oral phosphodiesterase 4 inhibitors (PDE4i) are commonly used to treat AD and psoriasis in many countries. However, their effects on MF/SS remain largely unknown, raising concerns about their potential impact in misdiagnosed cases or as therapeutics.

Methods, Results: In this study, we investigated the effects of apremilast, a representative PDE4i used for psoriasis, on CTCL cell lines (HH and Hut78) and peripheral blood mononuclear cells (PBMCs) isolated from patients with SS. *In vitro* assays demonstrated that apremilast inhibited cell proliferation in both HH cell lines (28% inhibition of cell proliferation at 100 ug/ml, $P = 0.002$) and Hut78 cell lines 26% inhibition of cell proliferation at 100 ug/ml, $P = 0.002$). Flow cytometric analysis of patient-derived PBMCs incubated with or without apremilast revealed that the CD4+CD7- malignant Sézary cell fraction was more significantly reduced compared to the CD4+CD7+ reactive T-cell fraction when incubated with apremilast. Furthermore, RNA sequencing and pathway analysis of HH cells treated with apremilast revealed an enrichment of the mitotic cell cycle process (GO:1903047). This suggests that apremilast suppresses cell activity broadly rather than inhibiting a single specific pathway.

Conclusion: These findings suggest that PDE4i have an inhibitory effect on malignant T cells that may be greater than their impact on reactive CD4+ T lymphocytes. Although the clinical significance of these results remains unclear, particularly with respect to the immune microenvironment and disease progression risk, they imply antitumor efficacy of PDE4i.

Learning Objectives:

The efficacy of PDE4 inhibitors against SS

9A.08 Management of Advanced Mycosis Fungoides and Sézary Syndrome: International Consensus Recommendations from EHA, EORTC-CLTG, ISCL and EBMT

Quaglino, Pietro[1], Onida, Francesco[2], Scarisbrick, Julia[3], Hodak, Emmilia[4], Willemze, Rein[5], Zain, Jasmine[6], Rindler, Katharina[6], SIlvia Alberti-Violetti, Martine Bagot, Lorenzo Cerroni, Amrita Goyal, Rudolf Stadler, Anna Sureda, Marco Ardigò, Emilio Berti, Adele De Masson, Rafael Palomino Duarte, Francine Foss, Eva Gonzales-Barca, Joan Guitart, Youn Kim, Pablo Ortiz-Romero, Evangelia Papadavid, Alessandro Pileri, Pierluigi Porcu, Miles Prince, Sima Rozati, Serena Rupoli, Maarten Vermeer, Sean Whittaker, Nicola Pimpinelli, Pier Luigi Zinzani

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Introduction: Advanced mycosis fungoides (MF) and Sézary syndrome (SS) represent the most aggressive forms of cutaneous T-cell lymphomas and remain associated with heterogeneous therapeutic strategies. In recent years, the therapeutic landscape has expanded considerably with the introduction of targeted agents and improved transplant strategies. Updated international guidance integrating dermatologic, hematologic, and transplant perspectives is therefore needed.

Methods, Results: An international multidisciplinary panel from four major organizations, the European Hematology Association (EHA), the EORTC Cutaneous Lymphoma Tumours Group (EORTC-CLTG), the International Society for Cutaneous Lymphoma (ISCL), and the EBMT Lymphoma Working Party, conducted a structured literature review and expert consensus process to develop recommendations for the management of advanced MF/SS. The consensus highlights a stage-adapted and compartment-oriented therapeutic approach. Immunomodulatory approaches remain central in advanced CTCL: extracorporeal photopheresis is commonly used as a first-line therapy in Sézary syndrome and in patients with significant blood involvement, while interferon-α and retinoids are widely used in mycosis fungoides across different disease stages, often in combination with skin-directed therapies. Targeted agents such as mogamulizumab and brentuximab vedotin represent key treatment options after prior systemic therapy, with differential activity across skin, blood, and nodal compartments. Combination strategies integrating systemic and skin-directed treatments may improve response depth and duration. Allo-HCT remains the only potentially curative option and should be considered early in selected patients with high-risk disease features.

Conclusion: These international consensus recommendations provide a practical framework for the multidisciplinary management of advanced MF and SS, supporting individualized treatment sequencing and early transplant evaluation.

Learning Objectives:

Guidelines for management

9A.09 Linking CTCL Cell Biology with Response to Mogamulizumab for Therapy Optimization and Identification of Resistance Mechanisms

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Introduction: Mycosis fungoides and Sézary syndrome belong to the heterogeneous group of primary cutaneous T cell lymphomas (CTCL). In 2018, the anti-CCR4 monoclonal antibody mogamulizumab (Moga) was approved for CTCL treatment. Currently, there is growing evidence on both primary and secondary therapy resistance. However, it has not yet been conclusively clarified which factors influence therapy response or may promote therapy resistance.

Methods, Results: 33 CTCL patients were included from five German dermatology centers belonging to the ADO lymphoma network. PBMCs and FFPE skin samples were collected at different time points: prior Moga-initiation, during Moga-therapy and at disease progression, as well as on the onset of Moga-associated rash (MAR). PBMC populations were analyzed by flow cytometry, while plasma proteins were examined via bead-based flow cytometric immunoassays. Alterations in the cellular signaling pathways implied in CTCL pathogenesis were analyzed with intracellular stainings. Furthermore, single-cell RNA sequencing was performed from 4 patients. This study was financially supported by Kyowa Kirin.

Analysis of the PBMC frequency showed a significant reduction in CCR4+CD4+ T helper cells as well as a modest decrease in FoxP3+CD4+ regulatory T cells during Moga-therapy independent of therapy response. In contrast, CD4+CD26- Sézary cell levels varied depending on therapy response and stayed constant or increased in non-responders. Besides, during Moga-therapy, a downregulation of the PI3K/Akt/mTOR signaling pathway was detected. The analysis of the cytokine and chemokine milieu revealed increasing levels of IL-10 and IL-22 in non-responding patients. Single-cell RNA sequencing revealed a loss of $CCR4^+$ T cells and an increased expression of Bcl-2 at the time of resistance.

Conclusion: This study aims to better characterize the biology of malignant CTCL cells and their skin microenvironment to identify predictors of Moga-therapy response and resistance. The observed upregulation of Bcl-2 might hint toward a possible combination therapy with venetoclax to overcome resistance mechanisms.

Learning Objectives:

Mogamulizumab resitance in CTCL upregulates Bcl-2 suggesting co-treatment with Bcl-2 inhibitors.

9A.10 Mapping the Spatial Immune Landscape in Sézary Syndrome: Insights into Moderate and Progressive Prognoses

Chevalier, Marie[1], Roggo, Andrea[2], IJsselsteijn, Marieke[1], van der Ploeg, Manon[1], Schrader, Anne-Roos[1], Merkus, Veerle[1], Tastanova, Aizhan[2], Levesque, Mitch[2], Dummer, Reinhard[3], Vermeer, Maarten[1]

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Introduction: Sézary syndrome is a rare (<5% of cutaneous T-cell lymphomas) and aggressive malignancy, with median survival of 32 months and 5-year survival of 10–30%. While blood involvement affects prognosis, the role of the skin tumour microenvironment (TME) remains unclear. Here, we analysed the spatial TME across patient samples with varying survival and potential prognostic markers.

Methods, Results: Spatial transcriptomics was performed on 18 FFPE baseline biopsies. Patients were stratified according to the median survival of Sézary syndrome (32 months). Those with survival above the median were classified as having a moderate prognosis if they were naïve to immunotherapy and/or chemotherapy (n = 5), or an intermediate prognosis if they had previously received these treatments (n = 4). Patients with survival below the median were categorized as having a severe prognosis (n = 6), including 4 who had been exposed to chemotherapy and/or immunotherapy and two who were treatment-naïve. In addition, four biopsies were collected from patients who progressed while receiving chemotherapy and/or immunotherapy, comprising 2 intermediate and 2 severe cases. Analyses used the Xenium platform (10x Genomics) with an immune-oncology panel (n=380) and a custom panel (n=95). Cell segmentation was performed with the Xenium Cell Segmentation Kit, and cell type annotation combined reference-based typing with clustering. Neighbourhood analyses were conducted using BANKSY and NicheCompass, with GRIDGENE applied to specifically examine the dermis–epidermis and dermis-vessels interfaces.

Spatial profiling of 18 samples suggests variation in immune and stromal cell organisation across prognostic groups, including differences in B-cell and cytotoxic T cell levels. Moreover, distinct spatial organisations of cells as well as different cell-cell interactions are observed between the cases.

Conclusion: Spatial mapping of Sézary syndrome reveals prognostic group–specific variation in the skin TME. Further analyses will determine how these spatial immune patterns relate to disease progression and outcomes.

Learning Objectives:

1. Understand the application of spatial transcriptomics to characterise the immune landscape in Sézary syndrome.
2. Recognise differences in immune and stromal cell organisation between patients with favourable and poor prognoses.
3. Appreciate the potential of spatial TME analyses to identify prognostic markers and guide therapeutic strategies.

SESSION 9B: PATIENT CASE VIEWING AND DISCUSSIONS IN CUTANEOUS LYMPHOMAS

9B.01 Clinical Spectrum and Diagnostic Challenges of Cutaneous T-Cell Lymphomas in Ghana: a Retrospective Analysis from a Tertiary Referral Center in Accra (2015–2024)

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Eastern Regional Hospital, Koforidua, Ghana

Introduction: Cutaneous T-cell lymphomas (CTCL) are rarely reported in sub-Saharan Africa, with data from West Africa particularly scarce. In resource-limited settings, CTCL is frequently misdiagnosed as infectious or inflammatory dermatoses due to overlapping clinical features, limited access to immunohisto chemistry, and lack of molecular diagnostics. This study aimed to define the clinical spectrum diagnostic challenges, and outcomes of CTCL in Ghana, highlighting features relevant to skin of color and low-resource environments.

Methods, Results: We performed a retrospective review of all patients diagnosed with primary or secondary cutaneous lymphoma at a tertiary referral center in Accra, Ghana, between January 2015 and December 2024. Diagnoses were established using clinicopathologic correlation and available immunohistochemistry (CD3, CD4, CD8, CD20, CD30, CD56, Ki-67). T-cell receptor gene rearrangement studies were not routinely available. Demographic data, clinical subtype, stage at diagnosis, HIV status, treatment modalities, diagnostic delay, and survival outcomes were analyzed. Forty-two patients were identified (median age 48 years, range 12–82; male-to-female ratio 1.8:1). Mycosis fungoides (MF) was the predominant subtype (71.4%), followed by Sézary syndrome (9.5%), primary cutaneous anaplastic large cell lymphoma (7.1%), and adult T-cell leukemia/lymphoma (4.8%). Hypopigmented MF constituted 40% of MF cases. Advanced-stage disease (≥IIB) was present in 61.9% at diagnosis. HIV co-infection was documented in 19%. Immunohistochemistry was performed in 64% of cases, primarily limited by cost and reagent availability. The median diagnostic delay was 28 months (range 3–96). Five-year overall survival was 42%, with significantly poorer.

Conclusion: CTCL in Ghana commonly presents late, affects relatively younger patients, and frequently manifests as hypopigmented MF, a variant that may be under-recognized in skin of color. Diagnostic delays driven by resource constraints substantially impact outcomes. Strengthening regional pathology capacity, expanding access to immunohistochemistry, and improving clinician awareness of CTCL variants are essential to improving diagnosis and survival in low-resource settings and have relevance for similar populations globally.

Learning Objectives:

To recognize region-specific clinical patterns and diagnostic barriers of cutaneous T-cell lymphomas in a resource-limited West African setting and their implications for global CTCL practice.

9B.02 Ocular Mycosis Fungoides: a Single Center Case Series

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Introduction: Ocular involvement in mycosis fungoides (MF) is rare and typically associated with advanced-stage disease. It may be associated with immunophenotypic switches, CNS involvement and poor outcomes.

Methods, Results: We retrospectively reviewed 3,043 patients with MF evaluated at MD Anderson Cancer Center between 1980 and 2023. Fourteen patients with ocular involvement were identified. Ocular MF was defined as radiographic or biopsy-proven intraorbital disease; eyelid and extra-orbital involvement were excluded. Clinical characteristics, treatments, responses, and outcomes were analyzed.

Median age at ocular involvement was 66 years, with a male predominance (9:5). Affected intraorbital structures included vitreous humor (43%), conjunctiva (14%), extraocular muscles (14%), optic nerve (14%), and orbital connective tissue (14%). Common presenting symptoms were floaters (43%), decreased visual acuity (36%), and blurry vision (29%); 71% had bilateral involvement. Most patients had advanced-stage disease at ocular involvement (85%), though two had stage I disease. Large cell transformation was present in 57%. Ten patients received orbital radiation (12–36 Gy), achieving an overall response rate of 80%, and two received intravitreal methotrexate.

Among patients evaluated for CNS disease, 80% demonstrated CNS involvement. Immunophenotypic shifts were observed in 57% of patients. One-year overall and disease-specific survival was 21%.

Conclusion: Ocular MF is an uncommon but ominous manifestation frequently associated with CNS involvement, immunophenotypic shifts and poor prognosis. Although radiotherapy provides temporary local control, survival outcomes remain poor. Early recognition, bilateral ocular evaluation, and CNS assessment are critical, even in patients with otherwise limited cutaneous disease.

Learning Objectives:

1. Ocular MF is frequently associated with immunophenotypic switches
2. Ocular MF is frequently associated with CNS disease
3. Degree of skin involvement may be incongrous with visceral ocular disease

9B.03 Recurrent Bulky Tumors in a Post-Allogeneic Stem Cell Transplanted Mycosis Fungoides Patient Cleared with a Single Dose of Pembrolizumab

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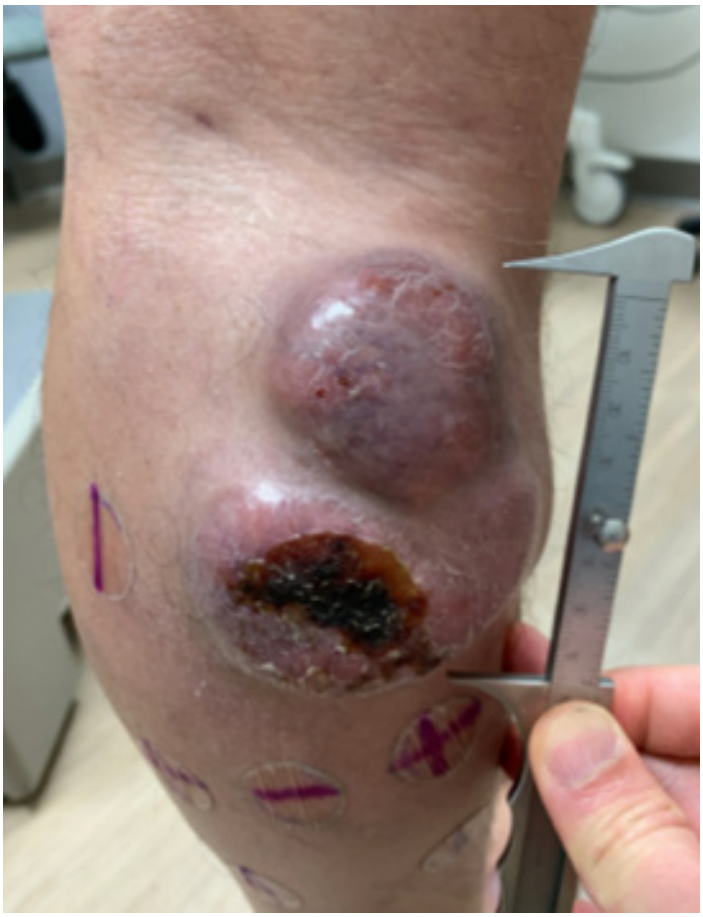
1. University of Virginia School of Medicine, Charlottesville, VA, USA, 2. Inova Health System, Fairfax, VA, USA

Introduction: We report a challenging case of Stage IIB transformed Mycosis Fungoides with explosive tumors after allogeneic stem cell transplant, successfully treated with one dose of pembrolizumab. Case discussion highlights strategic sequencing of targeted and immunomodulatory therapies.

Case Report: A 62-year-old man with history of Stage IIB (T3, N1, M0, B0b) Mycosis Fungoides with large cell transformation underwent allogeneic stem cell transplant in 2018. In 2019, he developed many painful necrotic subcutaneous masses, up to 8cm in diameter. Donor lymphocyte infusions were ineffective. His disease was well controlled with multiple cycles of combination brentuximab and focal radiation for five years until he reached cumulative exposure limits. Tumors showed high tumor mutational burden (10.5 and PDL-1 high) and he was treated with a single dose of pembrolizumab 200mg IV. He experienced clinical and radiologic pseudoprogression with enlargement of multiple subcutaneous and nodal masses, severe lower extremity edema and profound fatigue. Thirty days after receiving pembrolizumab, all lesions completely regressed clinically and radiologically.



Discussion: The patient's subcutaneous, large, almost pulsatile tumors represent an unusual disease morphology. The predictive value of PDL-1 and high tumor mutation burden was demonstrated in his dramatic response to an unprecedented single dose of pembrolizumab, compared with previously reported 25% overall response in large cell transformed Mycosis Fungoides.[1,2] His profound pseudoprogression resolved without complication despite concern for major immune-related adverse events (iRAE) with post-allo SCT data showing 62% 18-month progression-free survival but 33% iRAE with pembrolizumab.[3]

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Learning Objectives:

1. To describe an unusual clinical presentation of very large, entirely subcutaneous tumors in a patient with large cell transformed Mycosis Fungoides.
2. To highlight a dramatic complete response to a single dose of pembrolizumab in aggressive recurrent bulky tumor stage disease.
3. To explore the impact of PD-1 inhibitor exposure after allogenic stem cell transplant in Mycosis Fungoides and discuss considerations when sequencing immune modifying therapies.

9B.04 New Recalcitrant Perigenital Tumor in the Setting of Otherwise Well-controlled Sézary Syndrome

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Introduction: Sézary syndrome is a rare and aggressive leukemic variant of cutaneous T-cell lymphoma (CTCL). Unusual patterns of localized, refractory tumor development following prolonged remission have rarely been described.

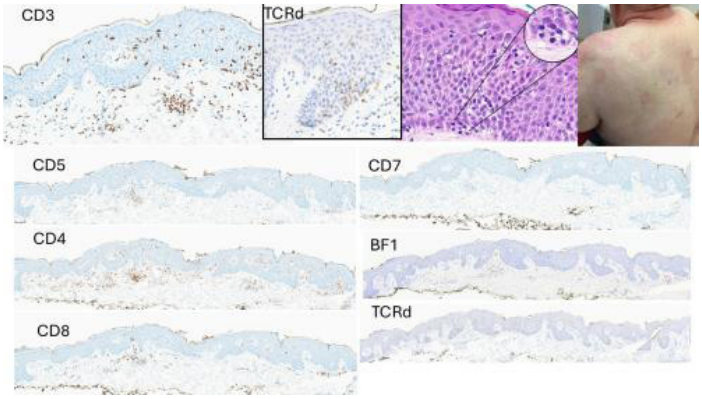
Case Report: We present a 61-year-old female patient with five-year history of stage IVA Sézary Syndrome (SS), who was in near complete remission for three years until the emergence of a recalcitrant perigenital ulcerated tumor.

Punch biopsy of the left buttock revealed a dense dermal infiltrate composed predominantly of large and pleomorphic lymphocytes, with the surrounding epidermis showing acanthosis and spongiosis with focal epidermotropism. Tumor cells were uniformly positive for CD3 and CD4 with weak CD30 expression. The biopsy confirmed recurrent cutaneous T-cell lymphoma (CTCL) with large cell transformation (LCT). PET/CT showed increased metabolic activity of the gluteal cleft and enlarged hypermetabolic lymph nodes.

The tumor was refractory to multiple treatment modalities, including targeted radiation therapy (27 Gy total), romidepsin, and pralatrexate. Repeat biopsy later revealed a superimposed Epstein-Barr virus-associated mucocutaneous ulcer with residual CTCL, further complicating management. Subsequent treatment with rituximab and BV-CHOP failed to produce clinical improvement, and progressive tumor extension into the perineum and labia necessitated diverting colostomy. Ultimately, combination chemotherapy with 3 cycles of gemcitabine (600 mg/m2) and etoposide (100 mg/m2) resulted in dramatic tumor regression and significant decrease in metabolic activity of the gluteal crease and perineum on PET CT.

This case highlights the diagnostic and therapeutic complexity of refractory CTCL tumors in anatomically sensitive sites, skin progression despite durable blood control, and the need for flexible, multimodal treatment strategies. Recognition of atypical tumor behavior despite systemic disease control is critical, and gemcitabine/etoposide-based regimens may represent a useful option in select refractory skin cases.


Clinical Images: Perigenital tumor before (left) and after (right) 3 cycles of gemcitabine (600 mg/m2) and etoposide (100 mg/m2).



Learning Objectives:

1. Participants should be able to understand the clinical challenges of treatment-resistant cutaneous T-cell lymphoma (CTCL) tumors in anatomically sensitive areas.
2. Participants should be able to recognize that disease progression can occur in alternate compartments even when the primary site of disease appears well-controlled.

9B.05 Epidermotropic Cutaneous T-Cell Lymphoma with Gamma Delta Immunophenotype: Four Instructive Cases

Junkins-Hopkins, Jacqueline

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Introduction: Primary cutaneous gamma delta T-cell lymphoma (PCGDTCL) is aggressive, usually presenting with ulcerated/crusted tumors/plaques/panniculitic nodules. Histology shows a predominantly dermal and subcutaneous immunophenotype that is CD3+/ TCR γδ+/ TIA1+ /beta F1(-). Epidermotropic MF-like presentations have rarely been reported. In contrast to MF, epidermotropic PCGDTCL may progress rapidly with an aggressive course or may be indolent.

Case Report: 15 year-old male with a solitary thin plaque on his flank/hip. Biopsy showed an epidermotropic CD3+TCRd+ lymphocytic infiltrate negative for CD4/CD5/CD7/CD8/BF1. He cleared with narrowband UVB and topical clobetasol and is free of disease at 10 years follow-up. A 67 year-old man presented in 2017 with several years of numerous dry patches with prior biopsies showing spongiotic dermatitis. Re-biopsy 2017 showed spongiosis and epidermotropic CD3+ lymphocytes (-) CD4/CD5/CD7/ CD8. He was lost to follow up without treatment until 2025, when he presented with numerous thin plaques on trunk/face/extremities, some eroded. Biopsy showed striking epidermotropism of lymphocytes that were (+) CD3/TCRd (-)BF1/CD2/CD4/CD5/CD8/UCHL1. A 73 year old man with history of X-linked ichthyosis presented with recent onset scaly patches and plaques on arms/back/thigh (10% body surface area) with background ichthyotic changes. A 70 year-old man on JAK inhibitor presented 2026 with thin scaly erythematous patches on the leg with histology showing mild spongiosis and beading epidermotropism with phenotype CD3+/TCRd+/CD5-/CD4-/CD8-/UCHL1-/BF1-. Similar patches biopsied 1 and 2 years prior showed spongiotic dermatitis with similar phenotype (performed later with recent biopsy).

Learning Objectives:

- Recognize features in biopsies from patients with MF-like presentations that may indicate gamma delta T-cell lymphoma, including loss of pan T-cell markers
- Patients with with epidermotropic gamma delta T cell lymphoma may do well for over 10 years, while others progress rapidly
- Become aware the epidermotropic primary gamma t-cell lymphoma may present as spongiotic dermatitis histologically

9B.06 Merkel Cell Carcinoma: A Cutaneous B-Cell Lymphoma in Disguise?

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Introduction: Merkel cell carcinoma (MCC) remains one of the most aggressive skin cancers, with limited treatment options and high mortality rates. The prevailing assumption that MCC originates from Merkel cells is increasingly questioned due to emerging molecular/clinical evidence. Emerging evidence suggests other potential origins for MCC, including hematological lineages.

Methods, Results: We utilized targeted and multi-omics approaches to explore gene expression patterns at protein and RNA levels of MCCs. Western blotting, immunofluorescence, and immunohistochemistry were performed using fresh and 92 FFPE samples of primary and metastatic MCC, and two MCC cell lines (MS-1, HaCaT). RNA sequencing of selected FFPE samples identified differentially expressed genes based on sex and Merkel cell polyomavirus (MCPyV) status. Finally, weighted gene correlation network analysis (WGCNA) and cell type enrichment analyses were employed to determine pathway and cell type enrichment, respectively.

MCC patient samples heterogeneously expressed B-cell and neuroendocrine markers and novel molecular targets including BCMA, CD10, CD93, PAX5, TdT, IgA, and CD19. Transcriptome analysis demonstrated differentially expressed genes based on sex and MCPyV status. MCPyV+ tumors had significant upregulation of genes involved in immune cell function and downregulation of processes related to neuronal activity. WGCNA highlighted enrichment for pathways involved in immune function, including B-cell

differentiation. Cell type enrichment analysis highlighted enrichment for multipotent stem cells, several immune cell types, and keratinocytes.

Conclusion: Our findings support previous studies which confirm that MCC is unlikely to be derived from Merkel cells and instead from multiple or divergent cell types, including those of B-cell lineage. This research provides a framework for future clinical investigations aimed at refining MCC diagnostics and developing targeted therapies, such as B-cell-directed treatments. By shifting the paradigm of MCC's cellular origin, this work proposes novel avenues for precision medicine strategies tailored to distinct molecular subtypes of this cancer.

Learning Objectives:

- Understand why Merkel Cell Carcinoma (MCC) was considered to be originating from Merkel Cells
- Evaluate molecular evidence of expression of hematologic, B-cell and other multipotent progenitors, epithelial cells, and keratinocytes in MCC tumors.
- Assess the evolving landscape of tumor heterogeneity and assess how it could be further exploited for therapeutic benefit in patients.

9B.07 Clinical Warburg Effect in a Primary Cutaneous Lymphoma

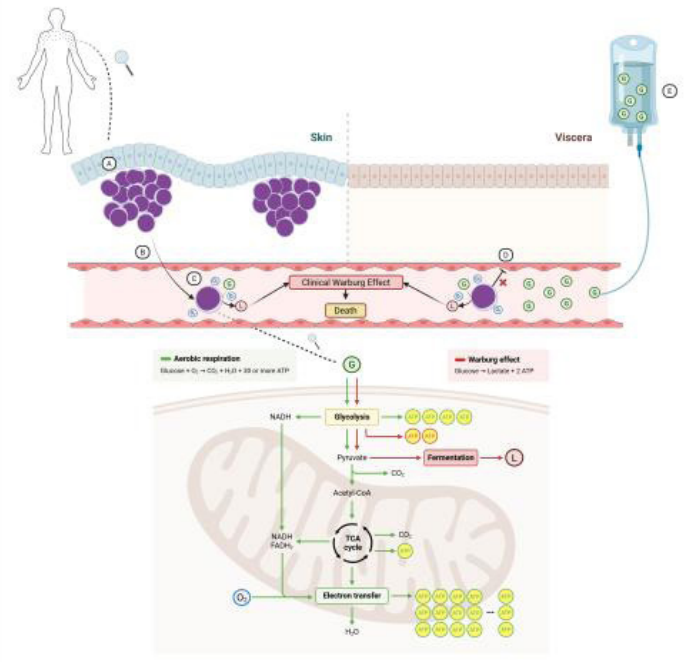
Martins, Francisco[1], Guenova, Emmanuella[2], Fontinha, Guilherme[3], Magalhães, José[4], Cardoso, José Carlos[1], Calvão, Joana[1]

1. Dermatology Department, University Hospital, Local Health Unit of Coimbra, Coimbra, Portugal, 2. Department of Translational Immunodermatology, Kepler University Hospital, Johannes Kepler University, Linz, Austria, 3. Anatomic Pathology Department of Coimbra University Hospital, Local Health Unit of Coimbra, Coimbra, Portugal, 4. Internal Medicine Department of Coimbra University Hospital, Local Health Unit of Coimbra, Coimbra, Portugal

Introduction: The clinical Warburg effect, classically reported in aggressive systemic lymphomas, is driven by sustained tumor glycolysis and may result in life-threatening hypoglycemia and lactic acidosis. We report a rare case of a primary cutaneous lymphoma manifesting with a clinical Warburg effect, highlighting the diagnostic challenges at the interface between primary cutaneous and intravascular lymphomas.

Case Report: An 84-year-old woman presented with a rapidly progressive eruption of indurated, violaceous nodules involving the face, cervicothoracic region, and upper limbs. During hospitalization, she developed refractory hypoglycemia with preserved oxygenation and profound lactic acidosis, leading to rapid death despite aggressive glucose and bicarbonate administration. Autopsy revealed a dense dermal and subcutaneous infiltrate consistent with diffuse large B-cell lymphoma, while multiple internal organs showed exclusively intravascular localization of neoplastic cells without parenchymal infiltration or mass formation. Although this pattern raised suspicion for intravascular large B-cell lymphoma, the predominantly extravascular cutaneous infiltrate, CXCR5 expression, and MUM1 negativity argued against this diagnosis, supporting primary cutaneous DLBCL, not otherwise specified, with secondary intravascular dissemination complicated by a clinical Warburg effect (Figure 1). Notably, glucose administration coincided with rapid clinical deterioration, likely by fueling tumor-driven glycolysis and exacerbating lactate production, underscoring the need for minimal metabolic support and urgent lymphoma-directed therapy in these cases.

This case underscores the need to conceptualize primary cutaneous lymphomas as biologically systemic diseases in which skin predominance reflects tissue tropism rather than true anatomic confinement. In aggressive presentations, unexplained hypoglycemia and lactic acidosis should prompt consideration of a clinical Warburg effect, as early recognition is critical given its fulminant and often fatal course.



Learning Objectives:

After this presentation, participants will be able to:

1. Recognize the clinical Warburg effect as a cause of refractory hypoglycemia and type B lactic acidosis in aggressive primary cutaneous lymphomas.
2. Recognize primary cutaneous lymphomas as biologically systemic diseases in which skin predominance reflects tissue tropism rather than true anatomic confinement.

9B.08 Cutaneous CD8+ Cytotoxic Gamma-Delta T-cell Lymphoma Mimicking Angioedema

Ostroff, Eleanor B.[1], De Jong, Katherine[1], Holm, JoJo[1], Trupiano, Nicole[1], Prenner, Joshua[2], Colavincenzo, Maria[1], Quan, Victor L.[1], Guitart, Joan[1], Zhou, Xiaolong A.[1]

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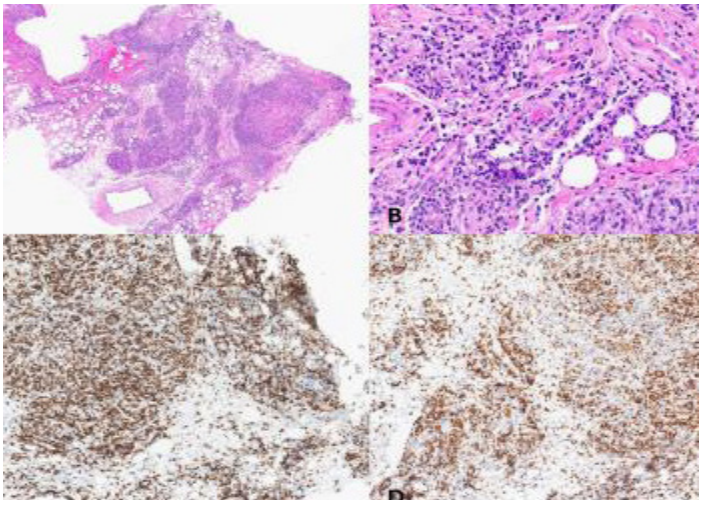
Introduction: Primary cutaneous gamma-delta T-cell lymphoma (PCGDTCL) is a rare but highly aggressive form of cutaneous T-cell lymphoma (CTCL). PCGDTCL has not previously been associated with angioedema-like presentation. We present a unique case of angioedema-like PCGDTCL.

Case Report: A 68-year-old woman with history of breast ductal carcinoma presented to clinic with ill-defined subcutaneous edema of the lower face. She reported nine months of facial swelling

that originated on the forehead and spread to the bilateral eyes and cheeks before shifting to the lower face. She was refractory to prednisone and levocetirizine. Prior work-up with Allergy/Immunology ruled out hereditary/acquired angioedema. Brain MRI was significant for edema and asymmetric enhancement of the right face involving the temporalis and zygomaticus muscles.

Lower lip biopsy revealed a deep dermal and subcutaneous infiltrate of small-to-medium sized atypical lymphocytes with hyperchromatic nuclei. Atypical lymphocytes rimmed adipocytes and nerves and demonstrated microvascular invasion of capillary vessels. CD3, CD8, granzyme, and TCR-delta were positive; cytokeratin, CD30, Beta-F1, and EBER were negative. Autoimmune panels were negative. PET/CT scan demonstrated lymphomatous uptake in the face, cranial nerves (V, VII-VIII), nasopharynx, sternocleidomastoid, bilateral trapezius muscles, right deltoid, and thoracic vertebrae T9-T11. The patient was diagnosed with Stage IV PCGDTCL and treated with systemic chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)) and local intralesional triamcinolone, with temporary clinical improvement.

We present this unique and challenging case of PCGDTCL with microvascular invasion mimicking angioedema. Cytotoxic PCGDTCL typically forms ulcerated tumors on the trunk/extremities and has not been previously associated with angioedema. As PCGDTCL often carries poor prognosis, early diagnosis is critical. Moreover, this case already exhibited peripheral nervous system involvement on PET/CT, making it difficult to treat, and angioedema-like presentation raises concern for potential airway compromise. We show this challenging case of PCGDTCL to highlight angioedema-like presentation as a possible manifestation of cytotoxic CTCL.



Learning Objectives:

Participants should be able to recognize that facial involvement by gamma-delta T cell lymphoma can mimic angioedema.

9B.09 Vulvar and Perianal CD8-Positive Lymphomatoid Papulosis: A Case for Interdisciplinary Management of Unknown Genital Lesions

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1. Department of Dermatology, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA, 2. Loyola University Chicago Stritch School of Medicine, Chicago, IL, USA, 3. Department of Pathology and Laboratory Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA, 4. Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA

Introduction: Lymphomatoid papulosis (LyP) is a rare CD30-positive lymphoproliferative disorder with a typically benign course rarely involving the mucosa. Mucosal lesions may be misinterpreted potentially delaying appropriate management. We present a case of CD8-positive vaginal and perianal LyP to encourage early clinical recognition and interdisciplinary care.

Case Report: A 57-year-old woman presented to gynecology with concern of a new tender lesion on the vulva present for two weeks. One year prior, she presented to outside dermatology for a pruritic neck rash, refractory to topical steroids, topical antifungals, oral antihistamines, and oral terbinafine. Biopsy of the neck demonstrated a CD30-positive lymphoproliferative disorder consistent with cutaneous LyP and subsequently referred to our oncology-dermatology specialty clinic.

At gynecology, extensive sexual health review of systems was negative. Exam demonstrated right labial, clitoral hood, and perianal eroded red-pink papulonodules, prompting vulvar punch biopsy. While awaiting final pathology results, the biopsy site became painful with malodorous drainage and gynecology recommended ibuprofen and topical antibiotic. Given gynecology's hesitance to initiate other therapies, the patient contacted her established oncology-dermatology LyP team. Dermatopathology revealed an atypical lymphohistiocytic infiltrate characterized by a CD8-positive, CD30-positive, CD3-positive, ALK-negative phenotype, confirming vulvar LyP and consistent with her prior neck biopsy results. Next generation sequencing (NGS), although negative for histiocytic mutations, was not covered by insurance. Our LyP team initiated topical clobetasol ointment twice daily for two weeks, then daily for two weeks and vaseline. Given persistent disease, she was uptitrated to a maintenance dose of methotrexate 15mg once weekly and narrowband UVB (NBUVB), which have successfully controlled her cutaneous and mucosal lesions.

This case emphasizes the importance for collaborative, interdisciplinary care in patients with known cutaneous LyP who present with new mucosal lesions. Early recognition may reduce symptom burden, prevent delays in care, and expensive diagnostic studies.

Chimenti S et al. J Am Acad Dermatol. 2001.

Learning Objectives:

1. To emphasize the importance of interdisciplinary collaboration between gynecology and dermatology in the management of atypical vulvar lesions to prevent diagnostic delay and avoid unnecessary surgical interventions.
2. Recognize lymphomatoid papulosis as a rare but benign CD30$^+$ lymphoproliferative disorder that can involve anogenital mucosal sites, including the vulva and perianal skin.

9B.10 CD8+ Primary Cutaneous Peripheral T-Cell Lymphoma in a 64-Year-Old Male: a Case Report and Diagnostic Insight

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Introduction: Primary cutaneous peripheral T-cell lymphoma, not otherwise specified (PC-PTCL-NOS), is a rare and aggressive cutaneous T-cell lymphoma that lacks defining clinical or histopathologic features and is often a diagnosis of exclusion. $CD8^+$ variants are particularly uncommon and pose a significant diagnostic challenge, as early lesions frequently mimic benign inflammatory or infectious dermatoses, leading to delayed recognition and disease progression. Reports of $CD8^+$ PC-PTCL-NOS remain scarce, especially from Southeast Asia. We present a case of $CD8^+$ PC-PTCL-NOS in a Filipino patient to highlight key diagnostic pitfalls and underscore the importance of early biopsy and comprehensive immunophenotypic evaluation.

Case Report: We report a case of $CD8^+$ primary cutaneous peripheral T-cell lymphoma, not otherwise specified (PC-PTCL-NOS), in a 64-year-old Filipino male who presented with progressively enlarging erythematous plaques and nodules on the trunk and extremities. Initial treatment with topical corticosteroids and empiric oral medications was ineffective. Skin biopsy revealed a diffuse dermal infiltrate of atypical lymphoid cells extending into the subcutis with minimal epidermal involvement. Immunohistochemical analysis demonstrated a $CD3^+$, $CD8^+$, $CD4^-$, $CD7^-$, $CD30^-$, $CD56^-$ phenotype with a high proliferative index, confirming $CD8^+$ PC-PTCL-NOS.

Baseline evaluation showed markedly elevated serum lactate dehydrogenase levels, with subsequent development of regional lymphadenopathy, indicating disease progression. Infectious and inflammatory etiologies were excluded through negative special stains, cultures, and slit-skin smears. The patient was referred for multidisciplinary management involving dermatology, hematology, and oncology.

This case underscores the aggressive nature and diagnostic complexity of $CD8^+$ PC-PTCL-NOS, particularly in its early stages when it may mimic benign dermatoses. Early biopsy, comprehensive immunophenotyping, and prompt systemic evaluation are essential to avoid diagnostic delay and guide appropriate management. To our knowledge, this represents the first reported case of $CD8^+$ PC-PTCL-NOS in a Filipino patient, adding to the limited global literature on this rare entity.

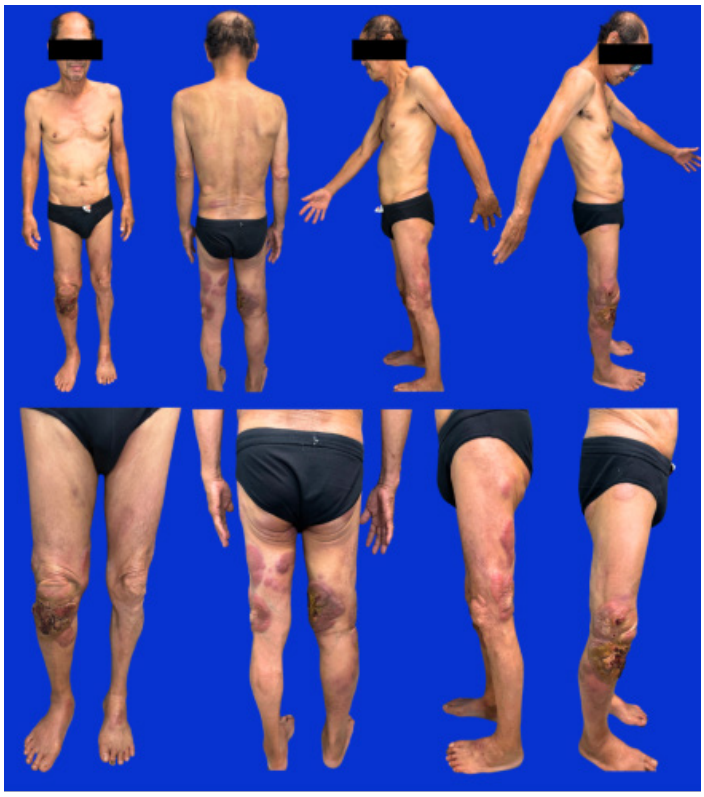

Figure 1. Baseline clinical presentation demonstrating multiple erythematous to reddish-brown plaques (0.5–3 cm) on the trunk, with coalescing violaceous to deep red plaques, nodules, and tumors (1–5 cm) on the bilateral lower extremities, some showing erosion, ulceration, hemorrhagic crusting, and mild exudation.

Learning Objectives:

1. Recognize the clinical and histopathologic features of $CD8^+$ primary cutaneous peripheral T-cell lymphoma, NOS, including its potential to mimic benign inflammatory dermatoses.
2. Describe the role of early skin biopsy and immunohistochemical profiling in the diagnosis of rare aggressive cutaneous T-cell lymphomas.
3. Discuss the importance of multidisciplinary evaluation and systemic staging in suspected aggressive cutaneous lymphomas.

ABSTRACTS: POSTER PRESENTATIONS

CHALLENGING CASES OF CUTANEOUS LYMPHOMAS

P01 Importance of Excisional Biopsy for Diagnosing EBV-Positive Diffuse Large B-Cell Lymphoma, Not Otherwise Specified Presenting with Extensive Histologic Necrosis

Hamada, Toshihisa[1], Kondo, Ryo[1], Kurakata, Akiomi[1], Hayashi, Yuichiro[2], Yamada, Takehiro[1], Uchida, Momoka[1], Arase, Kotono[1], Sekine, Chikako[3], Sugaya, Makoto[1]

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Introduction: EBV-positive diffuse large B-cell lymphoma, not otherwise specified (EBV+ DLBCL, NOS) is an aggressive B-cell lymphoma characterized by a polymorphous infiltrate with EBV-positive neoplastic B-cells. The histological features can mimic infectious disorders or reactive lymphadenopathy, leading to diagnostic delays. We report a case of an elderly patient who required three separate biopsies before the diagnosis of lymphoma.

Case Report: An 81-year-old Japanese male presented with a subcutaneous nodule in the left axilla. He had no history of treatment with immunosuppressants, including methotrexate. Fine needle aspiration of the nodule revealed aggregates of neoplastic cells positive for CD20, CD30 and EBER-ISH, suggesting Hodgkin lymphoma or EBV+ DLBCL, NOS; however, a definitive histological diagnosis could not be made. Subsequently, we attempted an incisional biopsy, but the specimen consisted largely of necrosis histopathologically, failing to yield a definitive diagnosis. Thereafter, the subcutaneous nodule gradually enlarged with deep ulcer formation. Five months after the incisional biopsy, the patient was referred to our department again due to severe pain and an intractable ulcer with no response to antibiotic treatments. CT scanning revealed a 4-cm mass in the left axilla and enlargement of deep lymph nodes. One month later, we resected the axillary subcutaneous mass under general anesthesia, leading to a pathological diagnosis of EBV+ DLBCL, NOS. Due to the patient's poor performance status, best supportive care was selected. He died of lymphoma two months after the diagnosis. The EBV-positive neoplastic cells were positive for LMP-1 but negative for EBNA2, consistent with EBV latency II.

This case highlights the diagnostic pitfalls of EBV+ DLBCL, NOS. Clinicians should consider EBV+ DLBCL, NOS in elderly patients presenting with a progressive subcutaneous nodule suspicious for lymphoma, accompanied by histopathological necrosis. In cases of diagnostic difficulty, excisional biopsy is recommended to obtain an adequate tissue sample.

Learning Objectives:

1. Clinicians should consider EBV+ DLBCL, NOS in elderly patients presenting with a progressive subcutaneous nodule suspicious for lymphoma, accompanied by histopathological necrosis.
2. In cases of diagnostic difficulty, excisional biopsy is recommended to obtain an adequate tissue sample.

P02 From Benign to Neoplastic: Evolution of Cutaneous Lymphoid Hyperplasia Into Primary Cutaneous Marginal Zone Lymphoma

Granara, Martina, Baquero Rey, Jenny A., Geloso, Marianela L., Kohan, Dana, Mazzuoccolo, Luis D., Enz, Paula A.

HOSPITAL ITALIANO DE BUENOS AIRES, BUENOS AIRES, Argentina

Introduction: Cutaneous lymphoid hyperplasia (CLH) is a benign reactive lymphoid proliferation that may mimic primary cutaneous lymphomas. It is commonly associated with chronic antigenic stimuli and typically shows a polyclonal lymphoid infiltrate. Although CLH and primary cutaneous marginal zone B-cell lymphoma (PCMZL) are considered distinct entities, rare cases suggest a possible biological continuum.

Case Report: We report a 62-year-old man with no relevant medical history who initially presented in 2009 with a painless nodular lesion on the right temple. In 2020, a skin biopsy performed at another institution revealed CLH, and clinical follow-up was recommended. In October 2024, he was referred to our department due to lesion progression, presenting infiltrated erythematous–violaceous plaques involving the right temple and malar region, as well as a smaller lesion on the nasal dorsum. No palpable lymphadenopathy was detected.

Histopathological examination showed preserved epidermis and superficial and deep dermal nodular lymphoid infiltrates composed of small and scattered larger lymphocytes with few plasma cells. Immunohistochemistry demonstrated CD20 positivity in most lymphocytes, CD3 positivity in a minority, focal BCL2 co-expression, CD10 negativity, and focal BCL6 positivity. Molecular studies revealed polyclonal B- and T-cell populations, supporting the diagnosis of CLH.

The patient received four sessions of intralesional triamcinolone with partial response. Due to persistent disease and the appearance of new lesions, a new biopsy was performed. Histology revealed a dense dermal lymphoid infiltrate with diffuse and nodular patterns, with a predominance of CD20-positive cells, and molecular analysis demonstrated B-cell monoclonality, establishing the diagnosis of PCMZL. Staging with PET/CT showed no extracutaneous involvement (T2bN0M0). The patient was treated with systemic rituximab (375 mg/m^2 weekly for four weeks), achieving complete clinical remission.

Learning Objectives:

This case highlights the rare progression of CLH to PCMZL and emphasizes the need for long-term surveillance, repeated biopsies in cases of clinical change, and close interdisciplinary collaboration.

P03 Extranodal Natural Killer/T-Cell Lymphoma, Nasal-Type, with Extranasal Cutaneous Presentation – Report of 3 Cases

Martins, Francisco[1], Guenova, Emmanuella[2], Cardoso, José Carlos[1], Calvão, Joana[1]

1. Dermatology Department, Local Health Unit of Coimbra, Coimbra, Portugal, 2. Department of Translational Immunodermatology, Kepler University Hospital, Johannes Kepler University, Linz, Austria

Introduction: Extranodal NK/T-cell lymphoma (ENKTL) is a rare, aggressive T-cell lymphoma, more prevalent in Asian populations and classically involving the nasal cavity. However, it can also occur in Caucasian patients and present as extranasal disease (uncommon overall, with primary cutaneous involvement being particularly

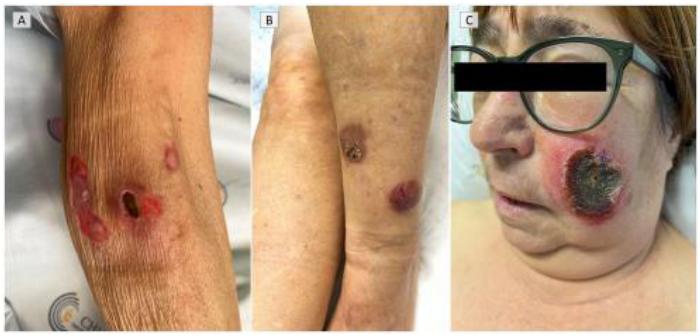
rare), where atypical clinical features complicate diagnosis and pose therapeutic challenges, especially in older patients or those with comorbidities.

Case Report: We present three Caucasian patients with primary cutaneous extranasal ENKTL diagnosed by skin biopsy, with in situ hybridization showing diffuse Epstein-Barr virus-encoded RNA positivity. PET-CT showed no suspicious extracutaneous lesions, apart from adenopathies in the third patient.

- Case 1: An 82-year-old man with asthenia and ulcerated lesions on the left leg and forearms (Figure 1A).
- Case 2: A 77-year-old woman with two erythematous nodules on the left leg, one with superficial ulceration (Figure 1B).
- Case 3: A 65-year-old woman with end-stage chronic kidney disease and a malar ulcer enlarging beyond 5 cm, later developing similar lesions on the limbs (Figure 1C).

The *SMILE* protocol (standard for ENKTL) was deemed unsuitable in all cases because of age and/or comorbidities. Reduced-intensity combination chemotherapy (*mini*-CHOP) was initiated in the first and third patients, while the second received a sandwich regimen with chemotherapy and radiotherapy (GemOx ×3, radiotherapy, GemOx ×3). The first and second patients are in complete remission for 2 and 1 years, respectively, whereas the third showed rapid progression with paraneoplastic pleural effusion and severe pancytopenia, dying two weeks after the first cycle.

These cases highlight that ENKTL should be considered in chronic, atypical ulcerated or nodular skin lesions regardless of ethnicity. Key lessons include the importance of early biopsy with EBV testing, exclusion of systemic disease, and individualized treatment strategies, as standard regimens are often unfeasible in older patients or those with comorbidities.



Learning Objectives:

After this presentation, participants will be able to:

1. Apply an appropriate diagnostic approach for suspected cutaneous ENKTL, incorporating skin biopsy, Epstein-Barr virus testing, and systematic exclusion of nasal and systemic disease.
2. Evaluate therapeutic options and prognostic considerations for cutaneous ENKTL in elderly or comorbid patients.

P04 Cutaneous T-Cell Lymphoma Developing in Surgical Scars Post Cardiac Surgery

Popradi, Gizelle[2], Michel, René P.[2], Skamene, Sonia[2], Lambert, Christine[2], Hijal, Tarek[2], Litvinov, Ivan V.[1]

1. St. Mary's Hospital Centre, McGill University, Montreal, QC, Canada, 2. McGill University, Montreal, QC, Canada

Introduction: Cutaneous T-cell lymphomas are a class of non-Hodgkin lymphomas characterized by the infiltration of malignant T cells into the skin. Their precise pathogenesis remains incompletely understood, but persistent and specific antigen stimulation of skin-homing CD4+ memory T cells by external or internal factors, combined with an inflammatory cytokine-rich tissue microenvironment, may be critical in the development of cutaneous T-cell lymphomas.

Case Report: We present herein a case of primary cutaneous T-cell lymphoma arising in two surgical scars that developed 6 months post-operatively and were successfully treated with external beam radiotherapy. This case highlights the notion that primary cutaneous T-cell lymphoma can develop locally at the site of injury/foreign body within a relatively short time post trauma/surgery. This work contributes to the literature of cutaneous T-cell lymphomas arising after a trauma, surgery, or a foreign body.

Learning Objectives:

- Understand how external triggers can promote pathogenesis of mycosis fungoides/CTCL
- Appreciate treatment outcome in these cases

P05 Long-term Development of Multiple Keratinocyte Malignancies Following Narrowband UVB Therapy for Mycosis Fungoides

Fujii, Kazuyasu, Kou, Aya, Yamamura, Yuto, Usui, Shunya, Otsuka, Atsushi

Kindai University Hospital, Sakai, Japan

Introduction: Narrowband ultraviolet B (NB-UVB) phototherapy is widely used in the management of mycosis fungoides because of its efficacy and favorable short-term safety profile. However, the long-term risk of secondary cutaneous malignancies following prolonged NB-UVB therapy remains incompletely characterized.

Case Report: A woman in her early sixties was diagnosed with mycosis fungoides (stage IIIA) after a prolonged history of erythrodermic skin lesions. She was treated with NB-UVB phototherapy for approximately seven years, receiving a total of 448 sessions with a cumulative dose of 170.5 J/cm^2, resulting in clinical improvement. Phototherapy was discontinued after keratotic lesions suggestive of actinic keratosis developed on non–sun-exposed areas. During the subsequent several years following discontinuation of NB-UVB therapy, she underwent repeated cryotherapy for multiple actinic keratoses. Approximately six years after cessation of phototherapy, she developed multiple keratinocyte malignancies, including squamous cell carcinoma, Bowen's disease, and bowenoid actinic keratosis, involving both sun-exposed and non–sun-exposed sites. Over a follow-up period exceeding a decade from initial diagnosis, she required repeated surgical excisions for recurrent and newly emerging lesions. Approximately eight years after discontinuation of phototherapy, disease flare of mycosis fungoides was observed, and treatment with bexarotene was initiated, leading to improvement of lymphoma-related skin symptoms. Despite adequate control of mycosis fungoides, new keratinocyte

malignancies continued to develop during long-term follow-up. There was no history of arsenic exposure, immunosuppressive medication, or other established risk factors for cutaneous squamous neoplasia. This case highlights a challenging long-term clinical course characterized by persistent development of multiple keratinocyte malignancies following prolonged NB-UVB therapy for mycosis fungoides, underscoring the need for careful risk–benefit assessment and prolonged dermatologic surveillance even after discontinuation of phototherapy and subsequent modification of lymphoma-directed treatment.

Learning Objectives:

1. To recognize the potential long-term risk of secondary keratinocyte malignancies following prolonged NB-UVB therapy for mycosis fungoides.
2. To understand the importance of cumulative ultraviolet dose and extended follow-up in phototherapy-treated patients.
3. To emphasize the need for long-term dermatologic surveillance even after apparent disease control in cutaneous lymphoma.

P06 Granulomatous Slack Skin–Like Cutaneous T-Cell Lymphoma in a 14-Year-Old With Hodgkin Lymphoma: A Rare Pediatric Presentation

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1. Geisinger Health System, Danville, PA, USA, 2. Children's Hospital of Philadelphia, Philadelphia, PA, USA

Introduction: Granulomatous slack skin (GSS) is a rare variant of mycosis fungoides characterized by granulomatous inflammation, multinucleated giant cells, and elastic fiber loss. Pediatric cases are uncommon, and ankle involvement is particularly unusual. GSS and interstitial MF may overlap histologically, requiring combined clinical, molecular, and immunophenotypic assessment.

Case Report: A 14-year-old male with stage IIB Hodgkin lymphoma presented with chronic bilateral ankle and foot lesions present for over three years. Clinical images demonstrated bilateral plum-colored to brown patches and thin plaques on the medial malleoli and dorsal-volar foot surfaces. Serial biopsies were performed, most recently in March 2025.

Microscopically, all specimens showed dense diffuse to nodular infiltrates of small lymphocytes mixed with epithelioid histiocytes and numerous multinucleated giant cells demonstrating emperipolesis. Mild nuclear irregularities were observed in less dense areas. In the acral biopsy, lymphocytes tracked along the epidermal base, and hemosiderin-laden histiocytes were present. Immunohistochemistry showed diffuse positivity for CD2, CD3, CD4, CD5, PD-1, and granzyme B, with near-complete loss of CD7 and only scattered CD8-positive lymphocytes. CD20 highlighted a small, admixed B-cell population; CD15, CD30, ALK, EMA, and EBER were negative. Ki-67 demonstrated a low proliferative index. Verhoeff–Van Gieson staining showed loss of elastic fibers within the involved dermis without overt elastophagocytosis.

Molecular analysis revealed matching monoclonal T-cell receptor gamma rearrangements in the knee and ankle biopsies, confirming clonal relatedness and supporting a diagnosis of cutaneous T-cell lymphoma. This case represents an uncommon pediatric cutaneous T-cell lymphoma with granulomatous slack skin–like features, acral involvement, and coexisting Hodgkin lymphoma. The evolving histopathology across serial biopsies highlights the challenges of distinguishing GSS from granulomatous or interstitial MF. Continued longitudinal surveillance is essential given the potential for progression or transformation.

Learning Objectives:

- To report a rare pediatric case of granulomatous slack skin–like cutaneous T-cell lymphoma with acral involvement and concurrent Hodgkin lymphoma.
- To illustrate the diagnostic challenges posed by overlapping histologic features with granulomatous and interstitial mycosis fungoides and underscore the value of integrated clinicopathologic and molecular evaluation.

P07 Langerhans Cell Histiocytosis (LCH) with Unusual Skin Presentation: a Dangerous Mimic of Erythrodermic Primary Cutaneous T-Cell Lymphoma/Sézary Syndrome

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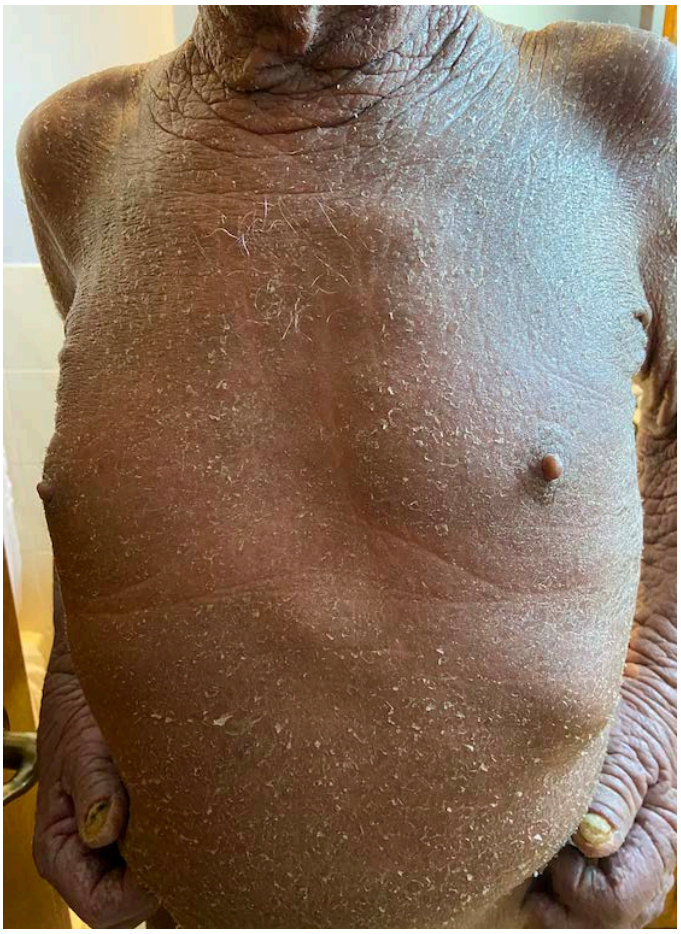
Introduction: On lists of causes of adult erythroderma, LCH is rarely included. LCH usually involves children and frequently manifests as diffuse papulonodular lesions. We report the case of a 72-year-old male referred to our cutaneous lymphoma clinic with 5-month history of erythroderma; swelling of face, torso and extremities; and hyperkeratotic fissuring of palms and soles; intractable pruritus; and weight loss.

Case Report: Peripheral blood eosinophilia and hypoalbuminemia were noted. Multiple skin biopsies showed non-specific mild-to-moderate superficial perivascular T-cell lymphocytic infiltrates with frequent eosinophils, without significant lymphocytic atypia or epidermotropism. PB (peripheral blood) lymphocyte count was within normal range. However, flow cytometry showed that 93% of lymphocytes were CD3+ T-cells, 4% were CD56+ NK cells and 2% were CD19+ B-cells. Of the T-cells, 83% were CD4+ and 9% CD8+ (CD4:CD8 ratio of 9.2). CD4+ T-cells were CD5+, CD26+, CD28+, CD10-, CD2+, CD7+dim, CD30+dim. Subsequent FCM testing identified no TRBC-1 restricted T-cells. Extensive molecular testing (by NGS and BIOMED-2) of skin biopsies and PB were negative for T-cell clonality. Imaging (CT neck/abdomen/pelvis and PET scan) showed bilateral cervical, axillary and inguinal lymphadenopathy, mildly hypermetabolic. An inguinal lymph node biopsy revealed that the paracortex contained large cellular aggregates of LCs (CD1a+/Langerin+) exhibiting sinusoidal distribution, providing strong evidence for LCH as the cause of the patient's illness. Brain MRI showed loss of normal T1 hyperintensity of the neurohypophysis. Endocrinological workup showed prolactin 26.5 ug/L (normal range 2.7-16.9), testosterone 1.3 nmol/L (normal range 6.7-25.7) and normal cortisol and growth hormone levels. Treatments included topical corticosteroids, prednisone, acitretin, doxycycline, doxepin, methotrexate, phototherapy (narrow-band UVB), and dexamethasone, of which only systemic steroids were clearly efficacious. The patient's clinical course was complicated by MRSA bacteremia and discitis. He expired after surgery for the latter, before chemotherapy for LCH could be instituted.



Learning Objectives:

LCH can be a mimicker of erythrodermic MF/Sézary

P08 Unilesional Granulomatous Mycosis Fungoides: Case Report in a Young Patient

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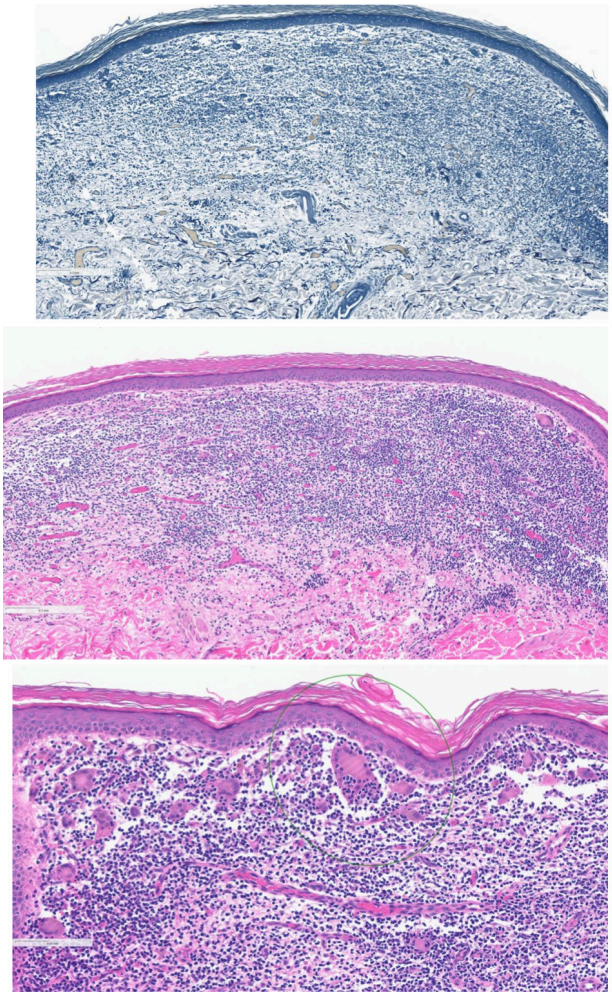
Introduction: Granulomatous mycosis fungoides (GMF) is a rare histological variant of cutaneous T-cell lymphoma, typically described in middle-aged men and usually presenting with multiple lesions. Unilesional presentation in a young woman is exceptional and may mimic benign granulomatous or melanocytic lesions, leading to diagnostic delay. This case highlights the importance of considering lymphoma even in atypical demographic and clinical settings.

Case Report: A 24-year-old woman presented with a solitary 6-mm pink papule on the arm clinically suspected as an atypical nevus; histopathology revealed an atypical CD3+, CD4−/CD8+ T-cell infiltrate with prominent granulomatous reaction, multinucleated giant cells and elastophagocytosis, consistent with GMF, with negative systemic staging. The patient was treated with topical corticosteroids and tacrolimus with good local response and no evidence of progression on follow-up. This case underscores that GMF may present as a single small lesion in young patients, emphasizing the need for a high index of suspicion and histologic evaluation of solitary granulomatous lesions to avoid misdiagnosis of this potentially aggressive lymphoma variant.



Learning Objectives:

1. To recognize the diagnostic challenges of rare variants of cutaneous T-cell lymphoma, especially in atypical patient population (such as young women with single lesions).
2. To appreciate the importance of biopsy and immunohistochemical analysis for accurate diagnosis and appropriate patient management.
3. To highlight the need for systemic staging after a GMF diagnosis to rule out extracutaneous disease, even in unilesional presentations.

P09 Cutaneous T-Cell Lymphomas Linked to Treatments with New Biological Agents and Small Molecules

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Introduction: Mycosis fungoides (MF), the most common cutaneous T-cell lymphoma, poses a diagnostic challenge due to its clinical and histopathological overlap with chronic inflammatory dermatoses, particularly atopic dermatitis (AD). The increasing use of biologic therapies and Janus kinase (JAK) inhibitors for moderate-to-severe AD has revealed cases of unmasking or progression of underlying cutaneous lymphomas. The aim of this report is to describe two cases of MF initially misdiagnosed as AD that evolved with erythroderma following targeted therapies

Case Report: We describe two patients with a prior diagnosis of AD who developed erythroderma after treatment with dupilumab and/or upadacitinib. Clinical features, histopathological findings, immunohistochemistry, flow cytometry, and staging studies were analyzed.

The first case involved a 27-year-old woman with chronic, refractory pruritic dermatosis who developed erythroderma and generalized lymphadenopathy after five months of upadacitinib therapy. Skin biopsies revealed epidermal and dermal infiltration by atypical lymphocytes with CD30 expression in a subset of cells, consistent with transformed MF. Flow cytometry identified a pathological T-cell population with a Sézary syndrome phenotype, and PET imaging demonstrated multistation nodal involvement, leading to a stage IIIB classification.

The second case involved a 56-year-old woman with long-standing dermatosis treated as AD, who developed erythroderma after dupilumab initiation and showed persistent disease under upadacitinib. Repeat skin biopsies confirmed plaque-stage MF, and flow cytometry demonstrated a predominant aberrant T-cell population compatible with Sézary syndrome, with nodal involvement on imaging, consistent with stage IV disease.

In both cases, discontinuation of immunomodulatory therapy and initiation of cutaneous lymphoma–specific treatments (interferon alpha, extracorporeal photopheresis, phototherapy, and/or total skin electron beam therapy) resulted in favorable clinical responses.

Learning Objectives:

MF should be considered in patients with refractory or atypical AD, particularly when paradoxical worsening or erythroderma occurs after targeted therapies. Early diagnostic reassessment with serial biopsies and immunophenotypic studies is essential to avoid diagnostic delay, prevent disease progression, and optimize patient outcomes

CLASSIFICATION / EPIDEMIOLOGY / PROGNOSTIC FACTORS

P10 Clinicopathologic Discordance in Folliculotropic Mycosis Fungoides: Clinical Relevance and Outcome Associations

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Introduction: Clinicopathologic discordance between clinical lesion appearance and histopathologic findings is common in folliculotropic mycosis fungoides (FMF). Prior studies have reported heterogeneous histopathologic features in FMF and conflicting data regarding their impact on clinical outcomes. As a result, clinicopathologic discordance is often assumed to reflect aggressive disease biology, yet its prognostic significance remains unclear. Clarifying whether discordance represents adverse risk or diagnostic complexity is critical for accurate clinical interpretation. In this study, we examined the relationship between lesion-level histopathologic features, clinical morphology, and overall survival in patients with FMF.

Methods, Results: Patients with FMF underwent lesion-level clinicopathologic correlation using the Folliculotropism–Intensity–Depth–Epidermotropism (FIDE) histopathologic framework. Clinicopathologic discordance was defined as mismatch between lesion-level clinical morphology and the extent of histopathologic involvement. Overall survival was evaluated using Kaplan–Meier estimates and Cox proportional hazards models in relation to discordance status and histopathologic involvement.

Among 33 patients with histologically confirmed folliculotropic mycosis fungoides, 18 patients with available in-house biopsy material were included in lesion-level clinicopathologic and survival analyses. Clinicopathologic discordance was not attributable to any single histopathologic feature or simple composite involvement score. Instead, discordance clustered in thin plaque lesions, while thick plaques and tumors were uniformly concordant. Within-patient analyses showed largely consistent histopathologic patterns across anatomic sites, suggesting less site-specific variability than previously implied. Overall survival did not differ by discordance status (log-rank $p = 0.60$; $n = 18$, events = 5), and histopathologic involvement, anatomic site, and lesion location were not independently associated with survival outcomes.

Conclusion: In this cohort, clinicopathologic discordance in FMF did not independently predict overall survival, indicating that discordant findings should prompt careful clinicopathologic correlation rather than be viewed as evidence of aggressive disease. Further stratification of thin plaque lesions by disease stage may help clarify whether lesion-level differences are associated with outcomes.

Learning Objectives:

1. Understand the clinical implications of clinicopathologic discordance in folliculotropic mycosis fungoides.

P11 B2 Mycosis Fungoides, Not Always Sézary

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Introduction: For many years Sézary syndrome (SS) was considered the leukemic variant of mycosis fungoides (MF). They might share some clinical features, but molecular and immunophenotypic studies demonstrate that they arise from different memory T-cell subsets.

SS is characterized by diffuse erythroderma, lymphadenopathy, and significant peripheral blood involvement. Rarely, MF can progress to a leukemic phase, fulfilling B2 staging criteria.

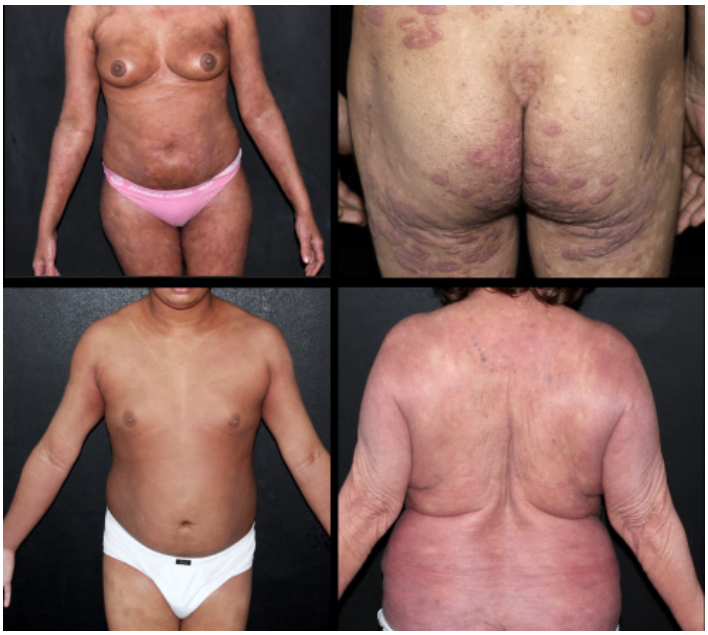
Methods, Results: The aim of this study is to describe a series of 6 cases of leukemic MF, and describe its clinical and immunephenotypical characteristics.

When analysing the clinical characteristics, came to our attention that 5/6 patients were diagnosed before age 35 (median age 31). There was a female predominance (4/6) and the median follow up was of

46.5 months (6 to 93 months). Two patients died of disease after 43 and 90 months, one is alive without disease (ongoing brentuximab treatment) and the other three patients are alive with disease, two of those, after allogenic stem cell transplantation.

Clinical caracteristics (will be illustrated on pictures): all patients developed at some point typical MF isolated plaques. Most of the cases developed blood involvement while they were "erythrodermic", if considering the definition of >80% of body surface area with erythema and scaling. However, looking carefully, it was in fact, confluent plaques covering >80%BSA. Keratoderma, alopecia, nail dystrophy were also rarely described.

Peripheral blood flow cytometry: relying solely on B2 initial definition, without absolute values, all patients fulfilled the B2 criteria, but only half of the patients had an absolute number of atypical cells >1000. All patients had a CD26-/CD4+>30% population, only two showed CD7-/CD4+>40% and 3/6 presented CD4/CD8 ratio>10. TCR monoclonal population was present at some point in all patients (blood and skin).



Conclusion: In conclusion, we demonstrated that B2 MF patients are distinct from Sézary.

Learning Objectives:

- Helping to differentiate B2 MF from SS patients.
- Highlinghting clinical and flow cytometry peculiarities.

P12 Prevalence of Human T Cell Lymphotropic Virus 1 Infection in Canada

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Introduction: Human T-cell lymphotropic virus type 1 (HTLV-1) is a chronic retroviral infection affecting an estimated 5–20 million individuals worldwide. Although endemic in regions such as the Caribbean, sub-Saharan Africa, South America, and parts of Asia, HTLV-1 remains a neglected infection in North America, where it is not nationally notifiable and population-level surveillance is limited. HTLV-1 is transmitted through blood exposure, sexual contact, and vertical transmission via breastfeeding. While most infected individuals remain asymptomatic, approximately 4–5% will develop adult T-cell leukemia/lymphoma (ATLL), an aggressive malignancy with poor prognosis. In Canada, the true prevalence of HTLV-1 infection is unknown. We sought to estimate the burden of HTLV-1 infection in Canada using national cancer registry and mortality data related to ATLL.

Methods, Results: We analyzed data from the Canadian Cancer Registry, the Registre québécois du cancer, and Vital Statistics databases to identify cases and deaths attributable to ATLL between 1992-2010. Incident ATLL cases and mortality were used to extrapolate the prevalence of HTLV-1 infection, assuming a lifetime ATLL risk of 4–5% among HTLV-1 carriers. Over the 18-year study period, ~200 ATLL cases and 75 ATLL-related deaths were identified nationwide. Based on these data, we estimated that 17,000–21,000 individuals in Canada are infected with HTLV-1, corresponding to a prevalence of 55–68 per 100,000 population. Quebec demonstrated the highest estimated prevalence (~109 per 100,000), likely reflecting immigration patterns from HTLV-1-endemic regions. Although routine screening of blood donors has reduced transfusion-associated transmission, these findings suggest a substantial burden of undiagnosed infection in the general population.

Conclusion: HTLV-1 infection is present in Canada and is associated with a quantifiable burden of adult T-cell leukemia/lymphoma. Estimates derived from national registry data suggest that HTLV-1 prevalence may be higher than previously appreciated. These findings provide epidemiologic context for HTLV-1 in Canada and may inform future efforts in surveillance, research, and clinical awareness.

Learning Objectives:

- Understand the epidemiology of HTLV-1 in Canada, including estimated prevalence and geographic distribution based on national cancer registry and extrapolation data.
- Recognize the clinical implications of HTLV-1 infection, including its lifelong nature and associations with adult T-cell leukemia/lymphoma and other serious conditions.
- Appreciate public health gaps in HTLV-1 surveillance in Canada and the need for enhanced screening and awareness to better characterize and mitigate disease burden.

P13 Clonal Granulomatous Dermatitis Associated With Myeloid Neoplasms: A Clinicomolecular Study of 16 Patients

Battesti, Gilles[1], Bozonnat, Alizée[1], Zhao, Lin Pierre[2], Mahévas, Thibault[1], Chasset, François[3], Gales, Lynn[3], Passet, Marie[4], Tournier, Emilie[5], Comont, Thibault[6], Michon, Adrien[7], Moguelet, Philippe[8], Sohier, Pierre[9], Jachiet, Marie[1], Lepelletier, Clémence[1], Cordoliani, Florence[1], De Masson, Adele[1], Itzykson, Raphael[10], Fenaux, Pierre[2], Raffoux, Emmanuel[10], Clappier, Emmanuelle[4], Bouaziz, Jean David[1], Battistella, Maxime[11]

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Hôpital Tenon AP-HP, Paris, France, Paris, France, 9. Pathologie, Hôpital Cochin, Paris, France;, Paris, France, 10. Hématologie adulte, Hopital Saint louis, Paris, France;, Paris, France, 11. Pathologie, Hôpital Saint-Louis AP-HP, Paris, France, Paris, France

Introduction: Granulomatous dermatitis (GD) sometimes occurs in the setting of myeloid neoplasms (MN), especially chronic myelomonocytic leukemia (CMML). However, the clonal link between MN and the associated GD has been exceptionally demonstrated. We aimed to describe the clinic-histological and molecular features of GD documented as clonally related to MN.

Methods, Results: This retrospective multicenter cohort study included 16 patients (Table, 56% male; median age at skin onset, 69 years) with GD, MN and at least one identical mutation in a gene recurrently mutated in MN in both hematopoietic and skin tissue. GD manifested as chronic plaques (73%), papules (69%), nodules (31%), or ulcerations (6%), usually involving two or more body segments (75%), and was associated with systemic granulomatous features in 36% of patients. Histopathologic patterns included unclassified (68%), granuloma annulare–type (28%), and palisaded neutrophilic GD (4%). Associated MN were mostly CMML and myelodysplastic syndrome (31%, each), acute myeloid leukemia and clonal cytopenia of undetermined significance (13%, each). In 13 patients (81%), GD preceded the diagnosis of MN; 12 of these (92%) showed blood count abnormalities at the time of GD diagnosis. Mutations of *SRSF2, IDH2* and *ASLX1* were the most frequent in skin and hematopoietic tissues. Among 26 evaluable treatment lines, cutaneous complete responses occurred in 14 (54%), partial responses in 5 (19%, overall response rate: 73%); progression in 6 (24%) and stable disease in 1 (4%). A myeloid clone-directed treatment allowed one complete and two partial responses.

Conclusion: GD may represent an early clonally related manifestation of diverse MN. These clonal GD are characterized by chronic and often diffuse papules, plaques, or nodules, BC abnormalities, histologically unclassified GD, high response rate to therapy and sometimes associated systemic granulomatous manifestations. Because clonal GD usually precede the MN diagnosis, blood count abnormalities should be assessed and investigated at the time of any GD diagnosis.

Table. Clinico-molecular characteristics and histological classification of 16 patients with myeloid neoplasm-associated granulomatous disease.

No. Sex, age	Clinical presentation	Histological classification (number of biopsy)	Systemic involvment of granulomatous disease spectrum	MN	GD preceding MN (delay, months)	Blood count disorder at time of DG diagnosis*	Targeted sequencing of blood or bone marrow (gene, VAF %)	Targeted sequencing of skin biopsy (gene, VAF %)	Treatment with available best response on skin	Follow-up duration (mounths)**, statues at last visit (last cutaneous statues)
1. F, 85	Nodules ; legs	Unclassified (2)	Arthralgia	MDS-IB1	No (61)	-	ASLX1 (43), RUNX1 (71), STAG2 (42), BCOR (36), NRAS (38)	ASLX1 (15), RUNX1 (14), STAG2 (8), BCOR (3), NRAS (3)	Azacitidine (CR)	4, death from COVID-19 disease
2. M, 63	Papules, plaques ; legs, trunk	Unclassified (2)	Uveitis, pericarditis	AML	Yes (8)	None	ASLX1 (48), SRSF2 (45), IDH1 (45), NRAS (34), NPM1 (28)	ASLX1 (19), SRSF2 (15), IDH1 (16), NRAS (12)	HCQ (P)	11, death from progressive sAML
3. F, 28	Papules, plaques, nodules ; face, legs	Unclassified (1)	Uveitis, scleritis, pachymeningitis	MPS	Yes (32)	Eosinophilia	ETV6::SYK tyrosine kinase fusion gene***	ETV6::SYK tyrosine kinase fusion gene***	Baricitinib (P) aHCT (CR)	50, death from sAML (occured 6 months after MPS diagnosis)
4. F, 69	Papules, plaques ; arms, legs, trunk, face	AG-type (2)	Uveitis	CMML	Yes (99)	Anemia, thrombopenia	SRSF2 (48), IDH2 (40), TP53 (9)	SRSF2 (13), IDH2 (12), TP53 (9)	HCQ + CS (CR) MTX (CR)	110, alive (CR)
5. F, 69	Plaques, ulcerations ; Face	Unclassified (2)	No	sLAM (after undiagnosed CMML)	Yes (4)	Neutrophils polynucleosis, monocytosis, lymphopenia	TET2 (52), DNMT3A (47), RUNX1 (5), NRAS (15)	TET2 (29), DNMT3A (17)	Azacitidine (PR)	9, death from progressive sAML
6. M, 78	Papules, plaques +/- annular disposition; arms, legs, trunk, face, scalp ; photodemarcation	Unclassified (2), PNGD (1), AG-type (1)	No	MDS LB	Yes (8)	Thrombopenia	SRSF2 (35), IDH2 (33)	SRSF2 (6), IDH2 (5)	HCQ (P)	10, death from cardiovascular event
7. F, 62	Plaques, +/- annular disposition ; legs, trunk, face	Unclassified (1), AG-type (1)	Uveitis, Arthralgia	CMML 2	Yes (12)	Anemia, lymphocytosis	IDH2 (10)	IDH2 (7)	HCQ + CS (CR)	34, alive (CR)
8. F, 72	Papules, plaques ; arms, trunk, face, scalp	Unclassified (1)	No	CMML	Yes (8)	Monocytosis	SRSF2 (43), IDH2 (32)	IDH2 (6)	CS (CR) CS + Interferon-alpha (P)	16, alive (P)
9. M, 61	Papules, plaques ; trunk	Unclassified (1)	No	CHIP	Yes (5)	Thrombopenia	TET2 (4), NFE2 (9)	TET2 (2), NFE2 (3)	HCQ (P) ; Infliximab (CR)	16, alive (CR)

Learning Objectives:

- Clonal granulomatous dermatitis (defined by the occurrence of granulomatous dermatitis, myeloid neoplasm (MN) with same clonal mutations profile in both skin and hematopoietic tissue in the same patient) is characterized by chronic and often diffuse papules, plaques, or nodules, and mostly precede the diagnosis of various myeloid neoplasm in patient with blood count abnormalities at time of dermatological diagnosis.
- These results highlighting the need to assess and investigate blood count abnormalities at the time of any granulomatous dermatitis diagnosis.

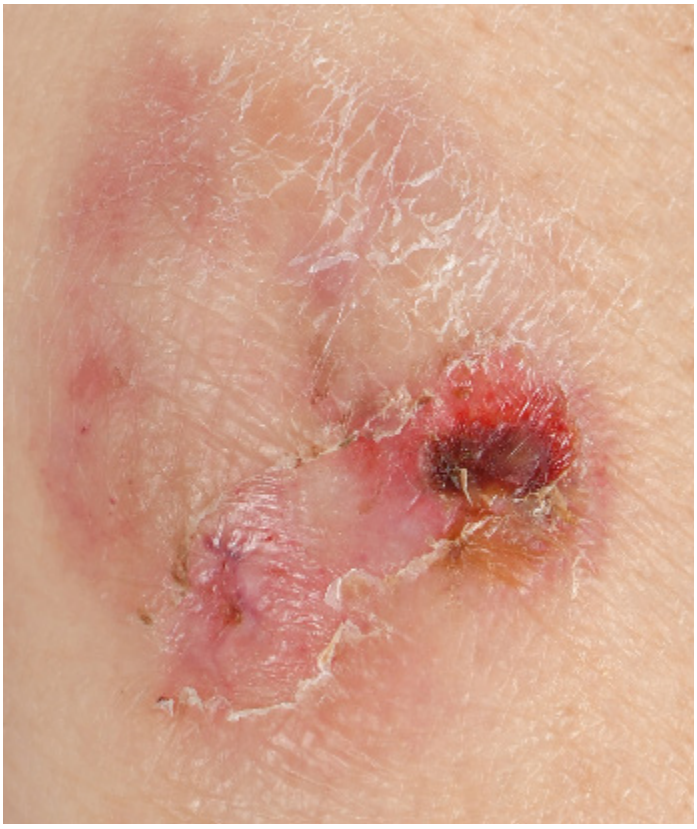
P14 Localised Primary Cutaneous Gamma-Delta T-Cell Lymphoma

Tee, Shang-Ian

National Skin Centre, Singapore, Singapore

Introduction: Primary cutaneous gamma-delta T-cell lymphoma (PCGDTCL) is an aggressive tumour with medial survival of 15-31 months and 10-20% 5-year survival rate. Patients usually present with disseminated plaques or tumours, along with B symptoms. We encountered a patient with a localised plaque that was histologically consistent with PCGDTCL, albeit with an indolent behaviour.

Case Report: A 51 year old Chinese female presented with a plaque on her left forearm of 1 month duration (figure below). The lesion was otherwise asymptomatic. Punch biopsy revealed epidermotropism of small-to-medium sized atypical lymphocytes, which also diffusely infiltrate the dermis. These show prominent angiocentricity. The cells expressed CD2, CD3, CD56, TCR-delta, TIA-1 and granzyme B. Beta F1, CD30 and EBER were negative. PET/CT scan did not reveal extracutaneous or nodal involvement. She was diagnosed with localised, indolent PCGDTCL. Treatment was instituted with localised radiotherapy followed by romidepsin. As the lesion regressed and she showed no signs of progression, stem cell therapy was held off. She remains in clinical remission 29 months from diagnosis.



Learning Objectives:

1. Recognise that classically aggressive cutaneous lymphomas may exceptionally present with indolent variants, potentially causing a pitfall and delay in diagnosis.
2. Appreciate that conservative measures may be instituted in such situations, given the toxic nature of aggressive systemic therapy.
3. Understand that aggressive transformation may still arise and patients should monitored closely.

P15 Primary Cutaneous B-Cell Lymphomas: A 13-Case Series from a Referral Center in Buenos Aires, Argentina

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Hospital Italiano de Buenos Aires, CABA, Argentina

Introduction: Primary cutaneous B-cell lymphomas (PCBCL) are uncommon lymphoid neoplasms arising in the skin without extracutaneous involvement at diagnosis, according to the WHO–EORTC classification. Clinical behavior and prognosis vary by histological subtype, making accurate clinicopathological and immunohistochemical correlation essential. Data from Latin America remain limited

Methods, Results: A retrospective, descriptive observational study was conducted including patients with histopathologically confirmed PCBCL treated between 2010 and 2025. Classification followed WHO–EORTC criteria. Demographic characteristics, histological subtype, lesion distribution, initial staging, treatment modalities, and clinical outcomes were analyzed.

Thirteen patients were included, with a mean age of 70 years (range: 57–90) and a slight female predominance (7:6). Histological subtypes included primary cutaneous marginal zone lymphoma (PCMZL) (n=6), primary cutaneous follicle center lymphoma (PCFCL) (n=3), and primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT) (n=4).

Therapeutic strategies comprised intralesional corticosteroids, surgical excision, radiotherapy, rituximab, and systemic chemotherapy (R-CHOP), depending on histological subtype, disease extent, and patient comorbidities. During follow-up, nine patients achieved complete response, two experienced relapse, and three showed disease progression. No lymphoma-related deaths were recorded. One patient with PCMZL developed secondary nodal involvement.

Conclusion: This series demonstrates a predominance of indolent PCBCL subtypes, consistent with international reports. Histopathological subtype remains the main prognostic determinant and the cornerstone guiding therapeutic decision-making. Reporting regional case series contributes to improving epidemiological knowledge and optimizing the management of these rare lymphomas in Latin America.

Learning Objectives:

To describe the clinical, histopathological, therapeutic features, and outcomes of patients with PCBCL treated at a referral center.

P16 Candidate Tumor Markers of Cutaneous T-cell Lymphomas Identified Through Analysis of Two Cases of Peripheral T-Cell Lymphoma, Not Otherwise Specified

Honda, Ryoma, Sugaya, Makoto, Hamada, Toshihisa

International University of Health and Welfare Graduate School of Medicine, Narita, Japan

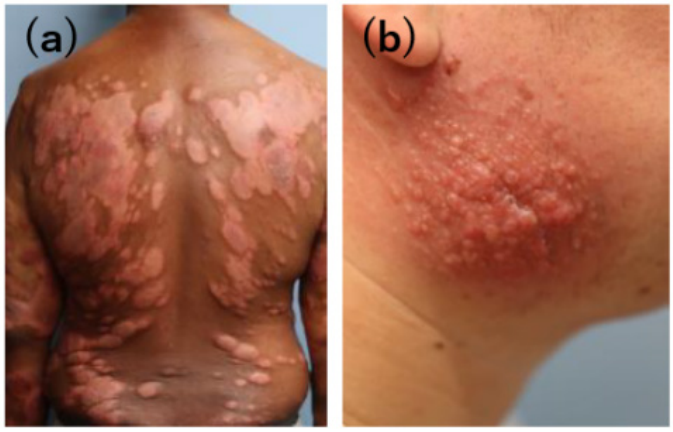
Introduction: We performed whole-genome sequencing (WGS) and RNA sequencing (RNA-seq) analyses using lesional skin samples from two cases of peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS), which showed only cutaneous involvement.

Case Report:

Case 1: A 29-year-old man presented with an infiltrative erythematous lesion on the right lower jaw. Skin biopsy revealed dense infiltration of atypical lymphocytes with nuclear atypia throughout the entire dermis, accompanied by epidermotropism. The tumor cells were positive for CD3, CD4, CD8, and CD20, and negative for CD7 and CD30 ($CD3^+CD4^-CD7^-CD8^+CD20^-CD30^-$). No extracutaneous involvement was detected. The patient was treated with intensity-modulated radiotherapy (40 Gy), followed by oral bexarotene plus ultraviolet phototherapy. Subsequently, he underwent allogeneic peripheral blood stem cell transplantation.

Case 2: A 43-year-old man presented with multiple cutaneous nodules distributed over the entire body. Skin biopsy demonstrated infiltration of large lymphoid cells with prominent nuclei throughout the dermis. Immunohistochemical analysis showed that the infiltrating lymphocytes were positive for CD3 and CD8 and negative for CD4, CD20, CD30, and CD56 ($CD3^+CD4^-CD8^+CD20^-CD30^-CD56^-$). Positron emission tomography–computed tomography and bone marrow biopsy revealed no evidence of extracutaneous involvement. Partial remission was achieved with ultraviolet phototherapy and oral bexarotene. However, the disease relapsed, and the patient was referred to our department. Despite subsequent treatment with etoposide, mogamulizumab, and gemcitabine, the patient died approximately one year after his initial visit to our hospital.

WGS analysis identified single nucleotide variants and indels in the *CSMD1* gene in the tumor cells of both patients. Furthermore, RNA-seq analysis, including data from previous studies, demonstrated that *FBXO43*, *PEAR1*, and *SPRY4* were upregulated in PTCL, NOS and mycosis fungoides compared with normal skin, atopic dermatitis, and psoriasis, whereas *CSMD1* expression was downregulated. Our study suggests that these oncogenes and tumor suppressor genes are important in the development of cutaneous T-cell lymphomas.



Learning Objectives:

After this presentation, participants will be able to:

1. Understand clinicopathological features of pcPTCL, NOS.
2. Understand that WGS and RNA-seq data are useful tools for
3. detecting candidate tumor markers of cutaneous lymphomas.
4. Recognize that expression profiles of certain oncogenes and tumor suppressor genes in pcPTCL, NOS are similar to those of mycosis fungoides, which are distinct from inflammatory skin diseases.

P17 Primary Cutaneous Lymphomas and Lymphoproliferative Disorders in a Community-Based Oncology Network: Disease Spectrum and Secondary Malignancies

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Introduction: Primary cutaneous lymphomas and lymphoproliferative disorders comprise a heterogeneous group of lymphoid neoplasms with variable clinical behavior. Data describing disease spectrum and coexistence of secondary malignancies are largely derived from tertiary referral cohorts. We sought to characterize primary cutaneous lymphoid disorders and associated solid malignancies within a community-based oncology network.

Methods, Results: Methods: We performed an IRB-approved retrospective chart review of patients diagnosed with WHO-defined primary cutaneous lymphomas and selected cutaneous lymphoproliferative disorders within a single community-based oncology network between 2015 and 2025.

Results: Forty-four patients were identified (27 male, 17 female; median age 64 years, range 13–89). T-cell–derived entities accounted for 55% (24/44) and B-cell–derived entities for 45% (20/44). The most frequent diagnoses included mycosis fungoides (13/44), primary cutaneous follicle center lymphoma (9/44), and primary cutaneous marginal zone lymphoma (9/44). Less common entities included primary cutaneous anaplastic large cell lymphoma (4/44), Sézary syndrome (1/44), and other rare aggressive primary cutaneous T-cell lymphomas. No cases of lymphomatoid papulosis were identified. Secondary solid malignancies were present in 20% of patients (9/44), most commonly prostate, lung, breast, and melanoma, and occurred more frequently in patients with T-cell–derived entities (6/9) than B-cell–derived disease (3/9).

Conclusion: This study describes the real-world spectrum of primary cutaneous lymphomas and lymphoproliferative disorders within a community oncology setting, demonstrating a comparable representation of T-cell and B-cell entities. Secondary solid malignancies were observed in one-fifth of patients, with a predominance among T-cell–derived disorders. The absence of indolent CD30-positive lymphoproliferative disorders highlights potential gaps in capture of these entities and supports complementary integration of oncology- and dermatology-based datasets to improve comprehensive characterization of primary cutaneous lymphoid disease.

Learning Objectives:

1. Describe the distribution of primary cutaneous T-cell and B-cell lymphomas identified within a non-tertiary-based oncology setting.
2. Recognize the frequency and patterns of secondary solid malignancies in patients with primary cutaneous lymphoid disorders.
3. Discuss potential gaps in capture of indolent cutaneous lymphoproliferative disorders and implications for clinical characterization.

P18 Prognostic Value of Tumor Clone Frequency in Mycosis Fungoides

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Introduction: In skin biopsies of patients with mycosis fungoides (MF), a higher percentage of the dominant malignant T-cell clone within the T-cell infiltrate, defined as tumor clone frequency (TCF), is proposed as a poor prognostic indicator. We evaluated the prognostic value of longitudinally obtained TCF in MF patients treated at a tertiary referral center.

Methods, Results: This retrospective cohort study conducted at Thomas Jefferson University included patients with stage IA to IVB MF who underwent T-cell receptor (b and g) immunosequencing on lesional skin biopsy specimens (2019-2024; Adaptive Biotechnologies). Clinicopathologic features were analyzed with immunosequencing data to validate the prognostic role of TCF. There was a large degree of variability among the frequency of dominant malignant T-cell clones by anatomical location and throughout clinical courses (average percentage change 37.6% (n=31); 35.9% (n=41) respectively). We found no correlation between average or maximum TCF (β and γ) and established prognostic factors, including values of mSWAT, BSA, LDH, or CLIPi and CLIC scores. When we divided patients into low and high TCF (β and γ) groups, based on the previously reported cutoff point of 25, we did not detect a statistically significant difference in their mean mSWAT, BSA, and LDH. However, patients who received systemic treatment had higher average and maximum TCFb, not TCFg, compared to those who did not receive systemic therapies.

TCF Associations	Average TCFβ	Max TCFβ	Average TCFγ	Max TCFγ	Statistical Test
Jump mSWAT > 25%	0.72	0.51	0.32	0.47	T-test p-values
Systemic Treatment Received	0.03*	0.04*	0.35	0.18	
LDH > 225 U/L	0.70	0.75	0.98	0.91	
Early CLIPi	0.11	0.11	0.26	0.20	ANOVA p-values
Late CLIPi	0.32	0.32	0.26	0.31	
CLIC	0.11	0.07	0.07	0.06	
TCF Associations	Average TCFβ >25%	Max TCFβ >25%	Average TCFγ >25%	Max TCFγ >25%	Statistical Test
mSWAT	0.11	0.15	0.21	0.17	T-test p-values
BSA	0.10	0.14	0.19	0.16	
LDH	0.43	0.57	0.522	0.38	

BSA: Body Surface Area, mSWAT: Modified Severity Weighted Assessment Tool, LDH: Lactate Dehydrogenase, CLIC: Cutaneous Lymphoma International Consortium, CLIPi: Cutaneous Lymphoma International Prognostic Index

Conclusion: Our study highlights that TCF is likely dependent on the biopsy site, subject to sampling error, and changes throughout clinical course. This variability in TCF makes its real-time clinical application difficult. Once we used average and maximum TCF as proxies, we could not demonstrate any correlation between TCF values and disease metrics, except for the probability of receiving systemic treatment. These discrepancies call for an expert consensus on the optimal use of TCF in clinical practice.

Learning Objectives:

- To evaluate the clinical and prognostic utility of longitudinally obtained tumor cell frequency values in patients with mycosis fungoides

P19 Long-term Outcomes and Recurrence Patterns in Primary Cutaneous Marginal Zone Lymphoma and Primary Follicle Centre Lymphoma B-cell Lymphoma

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Introduction: Cutaneous B-cell lymphoma (CBCL) is a rare subtype of lymphoma presenting in the skin with three distinct histological subtypes of which primary cutaneous marginal zone lymphoma (PCMZL), primary cutaneous follicle centre lymphoma (PCFCCL) are indolent lymphomas where multiple skin recurrence may occur, but systemic spread is rare. Currently there is no specific staging system for CBCL rather there are classified using the non-mycosis fungoides TNM classification. As such it can be difficult to predict outcomes.

Methods, Results: We retrospectively collated and analysed data from 117 patients across two United Kingdom large specialist cutaneous lymphoma centres. Data on patients' demographics, TNM classification, response to treatment, skin and/or systemic re-occurrence and co-existing malignancy were included.

The cohort included 51 females and 66 males. There were 59 cases of PCFCCL and 58 cases of PCMZL. Mean age at diagnosis was 58 years. First-line management include radiotherapy (63%), observation (10%) and surgery (9%). A total of 79 patients had skin recurrence, with a median time to first recurrences of 35 months (n=65) and late recurrences of 100 months (n=14). Second-line management for skin recurrence primarily involved radiotherapy (51%), observation (15%) and topical (8%). Twenty patients had co-existing malignancies which include prostate cancer, haematological malignancies, melanocytic and non-melanocytic skin cancers and solid organ malignancies. The median follow up duration was 6.46 years for the entire cohort, with a mortality rate of 9.4%(n=11). Overall survival was 99.1%, 94.9% and 91.5% at 1, 5 and 10 years respectively.

Conclusion: We report a cohort of CBCL with approximately 50% patients had skin recurrence within three years supporting the need for long term follow-up. Despite skin recurrence and other co-existing malignancies, the overall survival of CBCL patients remains excellent and indistinguishable from an average 58-year-old in the UK.

Learning Objectives:

1. Understanding the presentation and timeline of skin recurrence of primary cutaneous marginal zone lymphoma and primary cutaneous follicle centre lymphoma.
2. Understanding the utilisation of first-line and second-line treatments at initial diagnosis of cutaneous B-cell lymphoma and skin recurrence.
3. Studying the total disease and overall survival in cutaneous B-cell lymphoma in the United Kingdom cohort.

P20 Mantle Cell Lymphoma with Cutaneous Involvement: a Systematic literature review

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Introduction: Mantle cell lymphoma (MCL) is a distinct mature B-cell non-Hodgkin lymphoma defined by t(11;14)(q13;q32) and cyclin D1 overexpression. Most patients present with advanced-stage disease and frequent extranodal involvement, particularly of the bone marrow and the gastrointestinal tract. Cutaneous involvement is rare. Evidence describing the clinical characteristics, treatment approaches, and outcomes of patients with cutaneous MCL is limited.

Methods, Results: We conducted a systematic search of PubMed, Embase, and Web of Science in accordance with PRISMA guidelines. Case-level data were extracted from case reports and case series describing cutaneous involvement by MCL. Extracted variables included demographic, clinical, histopathological, imaging characteristics and survival outcomes when available.

We identified 128 patients (38 from case reports; 90 from 9 case series). Interim analysis of case reports showed 71% were male and 29% were female with a median age of 70.5 years (47–84). In 65.8% of reported cases skin was the initial site of MCL diagnosis. Sites involved were heterogeneous and often multifocal. In single-patient entries, when tested the following positivity percentage were extracted CD20 (32/34) (94.1%), cyclin D1 (31/34) (91.2%), CD5 (23/34) (67.6%), and BCL2 (15/34) (44.1%); Ki-67 >50% was tested in 9/38 cases and was greater >50% (67%-95%) in all tested cases. When utilized PET scan detected cutaneous involvement in 60% of cases.

Conclusion: Cutaneous involvement by MCL is frequently associated with aggressive disease and poorer clinical outcomes. PET imaging underestimates skin disease. Dermatologists should play a critical role in the multidisciplinary, longitudinal management of patients with mantle cell lymphoma.

Learning Objectives:

1. Identify the demographic and clinical characteristics, treatments, and outcomes of patients with mantle cell lymphoma with cutaneous involvement.
2. Describe the histopathological and imaging features of cutaneous mantle cell lymphoma.

PATHOLOGY / BIOMARKERS / MICROENVIRONMENT

P21 Single-Cell-Resolution Spatial Transcriptome Profile and Prognostic Implication of Cancer-Associated Fibroblast in Early-Stage Mycosis Fungoides

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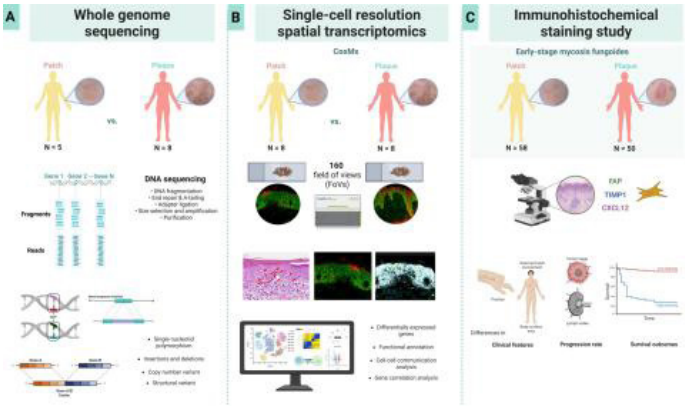
Introduction: Early-stage mycosis fungoides (MF) presents with patch or plaque lesions. Cancer-associated fibroblasts (CAFs) have been reported as abundant in early MF and may promote tumor proliferation and a Th2-predominant microenvironment. This study aimed to investigate genomic and transcriptomic alterations during progression from patch-MF to plaque-MF and to assess the prognostic implications of these changes in early-stage MF.

Methods, Results: Whole-genome sequencing was performed in 13 patients with early-stage MF. CosMx Spatial Molecular Imaging was used to analyze the single-cell-resolution spatial transcriptome from 8 patch and 8 plaque lesions. Immunohistochemical staining for CAF markers—FAP, TIMP-1, and CXCL12—was performed in 108 patients. Whole-genome sequencing demonstrated comparable single nucleotide, copy number, and structural variants between patch and plaque lesions. Spatial transcriptomics revealed fibroblasts as the dominant signaling sender in both patch- and plaque-MF. Plaque lesions exhibited expanded fibroblast-driven communication networks, including increased interactions with B cells and enhanced T cell chemotaxis. *CXCL12* was significantly upregulated in fibroblasts from plaque-MF and correlated with collagen gene expression and CCL19, key ligands mediating fibroblast-T cell signaling. T cells from plaque-MF also displayed increased *CXCL12* and *CCL19* expression and reduced expression of cytotoxicity-related genes. In the immunohistochemical cohort, high FAP and TIMP-1 expression correlated with poorer progression-free survival, whereas CXCL12 expression was associated only with tumor-stage progression.



Conclusion: This study highlights transcriptomic distinctions between patch-MF and plaque-MF at single-cell resolution and underscores the clinical and prognostic significance of CAFs in patients with early-stage MF.

Learning Objectives:

1. To understand the genomic profile of early-stage mycosis fungoides
2. To understand spatial transcriptomic changes during the progression of early-stage mycosis fungoides

P22 A Scoping Review on the Clinical Implications of the Skin Microbiota in the Therapy of Cutaneous T-cell Lymphoma

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Introduction: Cutaneous T-cell lymphoma (CTCL) is a rare and complex immunologic malignancy of the skin. Limited understanding of CTCL pathogenesis, including the tumor microenvironment's role, hinders treatment. Emerging evidence suggests that the skin microbiota can modulate disease in CTCL, with dysbiosis contributing to progression and representing a new therapeutic target. The objective of this scoping review was to investigate existing literature on the (1) composition of the skin microbiota in CTCL patients and (2) potential role of microbial-targeted therapies in improving clinical outcomes.

Methods, Results: A search of OVID's Medline and Embase databases was conducted to identify original articles evaluating the skin microbiota or microbial-based therapies in patients with mycosis fungoides and Sézary syndrome. Two independent reviewers screened titles and abstracts, then full texts, resolving discrepancies with a third reviewer. Review methodology adhered to the PRISMA-ScR guidelines.

Of the 2,336 records identified, 37 studies synthesizing data from >800 CTCL patients were included. Of the 17 articles addressing skin microbiota, majority of the articles analyzed bacterial composition, then viral and fungal. Staphylococcus aureus was the most examined species overall, and less than half of the studies assessing its abundance between CTCL lesional and healthy skin reported significant differences. Variability was driven by CTCL staging and subtype. Of the 21 articles addressing the clinical role of microbial-targeted therapies, several cases illustrated therapeutic synergy between antimicrobials and CTCL-directed treatments, especially for patients with S. aureus skin colonization, concomitant fungal infection, erythroderma, hyper-eosinophilia or lesions exhibiting ulceration and pustular inflammation.

Conclusion: Inconsistencies have precluded the establishment of a definitive association between skin microbiota compositions and CTCL. However, microbial-targeted therapies against critical colonizers or infections in adjunct to conventional CTCL therapies may improve patient outcomes. Given the burden of refractory disease among CTCL patients with dysbiosis, further investigation into host–microbe interactions are warranted.

Learning Objectives:

1. Understand current evidence assessing (1) alterations in the skin microbiota of patient with CTCL, and (2) the potential role of microbial-targeted therapies in improving clinical outcomes.

2. Heterogeneity in microbiota composition across studies have led to variable conclusions, influencing the consensus on microbial signatures in CTCL.
3. Microbial-targeted therapies, including antimicrobial agents and decolonization strategies, may serve as adjuncts to standard CTCL treatments to improve patient outcomes in specific clinical contexts, including erythroderma and hyper-eosinophilia.

P23 Diagnosis of Cutaneous Lymphomas by T-Cell Clonality Analysis: Comparative Effectiveness of Methods

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Introduction: Clonal T lymphocytes are descendants of a single lymphocyte and share identical antigen specificity and nucleotide sequences of rearranged T-cell receptor (TCR) genes. Rearrangements of TCR loci occur sequentially during T-cell development, beginning with *TRD*, followed by *TRG*, *TRB*, and *TRA*.

One of the major diagnostic challenges is the high rate of false-negative results at early stages of mycosis fungoides (33–48%), necessitating a comparison of the specificity and sensitivity of clonality assessment using capillary electrophoresis (CE) of the *TRG* and *TRB* loci, as well as an evaluation of the potential of high-throughput sequencing (HTS).

Methods, Results: The study included 161 skin biopsy samples analyzed by CE, and 31 skin biopsy analyzed by CE and HTS. CE results for the *TRG* and *TRB* genes were concordant in 88% (141/161) of samples: 71 TRG+/TRB+, 69 TRG-/TRB-, and 1 TRG+/-/TRB+/-. Analysis of discordant cases showed that in 14 of 16 cases with a monoclonal result at one locus, diagnosis of T-cell lymphoma was confirmed.

For comparison of CE and HTS, 14 skin samples and 11 peripheral blood samples from patients with mycosis fungoides, as well as 17 skin samples from patients with non-neoplastic dermatoses, were analyzed for *TRG* and *TRB* loci. Comparison of CE and HTS revealed no fundamental differences in clonality assessment between the two methods: patients with polyclonal CE results demonstrated diverse clonal repertoires by HTS with a dominant clone below 6.1%, whereas monoclonal CE results corresponded to the presence of a dominant *TRG* or *TRB* clone with an allelic burden exceeding 5.5% by HTS.

Conclusion: For clonality assessment in skin biopsies with suspected cutaneous T-cell lymphoma, CE analysis of the *TRG* locus is sufficient, with additional *TRB* testing recommended in cases of negative results. HTS is justified in early-stage mycosis fungoides with atypical aggressive disease course.

Learning Objectives:

T-cell clonality; capillary electrophoresis; high-throughput sequencing

P24 JAK-Inhibition As A Novel Multilevel Treatment Of Cutaneous T Cell Lymphoma

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Introduction: The Janus Kinase/Signal Transducer and Activator of Transcription (JAK/STAT) signalling pathway plays a central role in the pathogenesis of cutaneous T cell lymphoma (CTCL) and is frequently altered through point mutations as well as copy number gains. Accordingly, JAK inhibitors represent a targeted therapeutic strategy capable of suppressing aberrant JAK/STAT signalling and potentially limiting CTCL progression. This is an investigator-initiated, open-label phase I study primarily assessing the safety of systemic Tofacitinib, a pan-JAK inhibitor, in CTCL, with secondary evaluation of clinical and mechanistic effects.

Methods, Results: Eligible patients completed a study with up to 4 weeks of screening, 8 weeks of treatment with oral tofacitinib (10 mg twice daily), and 4 weeks of follow-up. Clinical outcomes, quality of life, skin samples, and molecular analyses were assessed at baseline and after 8 weeks of treatment. Despite similar clinical presentations at baseline, histopathological and STAT signalling patterns were different among patients. After eight weeks of treatment with Tofacitinib, decreased epidermal lymphocyte infiltration and lower numbers of $CD3^+$ and $CD4^+$ cells were observed in the lesional skin of 3 out of 7 patients. These patients exhibited epidermotropism, higher baseline p-STAT1 and p-STAT3 expression, and corresponding partial clinical responses to treatment, accompanied by a marked reduction in p-STAT1 and p-STAT3 levels after therapy. These three responder patients demonstrated a continuous drop over the 8 weeks in the Modified Severity-Weighted Assessment Tool (mSWAT) score indicating their clinical improvement. Moreover, total skin-index29 scores indicated decreased Health-Related Quality of Life (HRQL) impairment in all patients except patient one, reflecting an improvement in quality-of-life following therapy.

Conclusion: These findings indicate that activation of the JAK/STAT pathway, particularly elevated baseline levels of p-STAT1 is associated with increased sensitivity to Tofacitinib and may serve as a predictive marker for response to JAK inhibition with tofacitinib in CTCL

Learning Objectives:

Novel treatment, Drug resistance, Tofacitinib

P25 Phenotypic Switching in Mycosis Fungoides/Sézary Syndrome Patients: Clinical Implications and Survival Outcomes in Four Brazilian Cases

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Introduction: Advanced molecular biology techniques have shown that different clonotypes may be detected in different lesions from cutaneous T-cell lymphoma patients, revealing tumor heterogeneity within the same individual. However, phenotypic plasticity resulting in changes in immunophenotype characteristics in malignant cells is rarely described.

We report four mycosis fungoides (MF)/Sézary syndrome (SS) cases who developed different phenotypes along the follow-up.

Methods, Results: Table 1 summarizes the cases. There were two males and two females, median age at diagnosis of 55.8 years (45.7-59.0). Two patients had classic MF (stage T1aN0M0B0, stage T3N0M0B0), one folliculotropic MF (T2bN0M0B0), and one SS (T4N0M0B2). One patient (folliculotropic MF) developed large cell transformation. In immunohistochemistry analysis, switch from CD4+CD8- to CD4-CD8+ phenotype was observed in three patients,

and one presented switch from CD4+CD8- to CD4-CD8-. In three cases, the different phenotypes were detected in extracutaneous sites (two in the lymph nodes, one in paravertebral mass and corpus callosum). All patients received topical steroids, phototherapy, and multiple systemic agents prior to immunophenotypic change. All patients died due to progression of disease, with median overall survival of 7.2 years (1.9-19.3). Median time to phenotypic switch was 6.8 years (1.8-17.0). After phenotypic change, median time to death was 5.9 months (1.3-27.5).

Table 1. Characteristics of four patients with mycosis fungoides/ Sézary syndrome with phenotypic switch

	Age at diagnosis (years)	Sex	Diagnosis	Staging at diagnosis	Elevated LDH at diagnosis	Initial phenotype	Final phenotype	Overall survival (years)
1	52.8	F	Classic MF	T1aN0M0B0	No	CD4+CD8-	CD4-CD8- (lymph node)	8.0
2	58.7	F	Classic MF*	T3N0M0B0	No	CD4+CD8-	CD4-CD8+ (skin)	19.3
3	59.0	M	Folliculotropic MF	T2bN0M0B0	No	CD4+CD8-	CD4-CD8+ (paravertebral mass, corpus callosum)	6.5
4	45.7	M	Sézary syndrome	T4N0M0B2	Yes	CD4+CD8-	CD4-CD8+ (lymph node)	1.9

F: Female; M: male; LDH: lactate dehydrogenase; MF: mycosis fungoides

*Transformed MF

Conclusion: Phenotypic switch is rarely reported in MF/SS despite the known clonotype heterogeneity. Most switches occur from CD4+CD8- to CD4-CD8+. Studies suggest that phenotypic switch is a poor prognosis marker, especially from CD4-CD8+ to CD4-CD8-, or CD4-CD8- to CD4-CD8+. While the emergence of a second lymphoma cannot be excluded, studies demonstrating identical clonal populations despite phenotypic changes support immunophenotypic switching. This may represent clonal adaptation or accumulation of mutations driven by tumor microenvironment. Early detection of phenotypic changes is essential to alert for the need of close follow-up of MF/SS patients.

Learning Objectives:

- Recognize that phenotypic switching is uncommon, but a clinically significant phenomenon in MF/SS.
- Understand that phenotypic switching is associated with poorer prognosis.
- Emphasize the role of serial immunophenotyping in monitoring disease progression.

P26 Tumor-Informed ctDNA MRD Monitoring Correlates with Cutaneous Lesion Evolution and PET Response in Stage IIB Mycosis Fungoides

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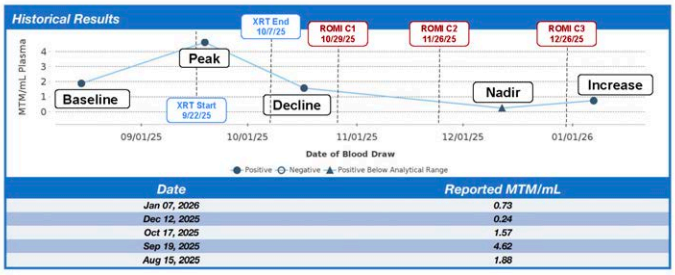
Introduction: Tumor-informed circulating tumor DNA (ctDNA) minimal residual disease (MRD) assays enable serial, quantitative disease tracking, but their role in cutaneous T-cell lymphoma (CTCL) is not well defined. We report a tumor-stage CTCL case highlighting ctDNA MRD kinetics measured as mean tumor molecules per milliliter (MTM/mL) alongside changes in cutaneous lesions and positron emission tomography/computed tomography (PET/CT).

Case Report: A 52-year-old woman was diagnosed with stage IIB mycosis fungoides/CTCL after biopsy of a tumor-stage chin lesion with additional facial involvement. Staging PET/CT showed hypermetabolic thickening of the chin and a small additional cutaneous focus without visceral disease. She received involved-site radiation to symptomatic facial lesions (completed 10/7/25) with marked clinical improvement, followed by systemic romidepsin (cycle 1 start 10/29/25; cycle 2 start 11/26/25; cycle 3 start 12/26/25). Given the desire for objective, quantitative monitoring beyond visual skin assessment, serial tumor-informed ctDNA MRD was obtained and trended with disease course: 1.88 MTM/mL (8/15/25) → 4.62 MTM/mL (9/19/25) → 1.57 MTM/mL (10/17/25, post-radiation) → 0.24 MTM/mL (12/12/25, after two cycles). Interim PET/CT (12/22/25) demonstrated complete metabolic resolution of the chin lesion and decreased uptake in the forehead lesion without new hypermetabolic sites; ctDNA subsequently rose to 0.73 MTM/mL (1/7/26) shortly after this imaging response, coinciding with newly documented patch/plaque involvement on 1/2/26 (right periorbital/orbital region and left nares), suggesting ctDNA may detect early disease recrudescence between interval imaging studies. Serial ctDNA MRD monitoring may complement skin examination and PET/CT by providing a quantitative signal of evolving cutaneous disease activity; prospective evaluation in CTCL is warranted.



XRT: Radiation
ROMI: Romidepsin

Learning Objectives:

- Describe how tumor-informed ctDNA MRD testing can be trended longitudinally in cutaneous T-cell lymphoma.
- Compare ctDNA MRD kinetics with clinical lesion burden and PET/CT metabolic response during multimodality therapy.
- Identify how ctDNA trends may complement skin examination and PET/CT in detecting response and emerging sites of disease.

P27 Dissecting Immune Determinants in Lesional Skins of Cutaneous T-Cell Lymphoma During Mogamulizumab Therapy

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Introduction: Mycosis fungoides (MF) and Sézary syndrome (SS) are the most prevalent cutaneous T-cell lymphomas (CTCL). Although malignant T cells in MF/SS overexpress CCR4 and respond to the FDA-approved anti-CCR4 antibody mogamulizumab, skin response rates remain limited. We hypothesize that immune components within the tumor microenvironment in MF/SS contribute to differential skin responses and therapeutic resistance.

Methods, Results: We performed imaging mass cytometry using a 37-antibody panel (31 validated) targeting immune and structural markers. FFPE tissues from sixteen patients (6 MF, 10 SS) in our prior study were analyzed, including 7 skin responders (43.8%) and 9 non-responders. Thirty-four ROIs (18 pre- and 16 post-treatment) were evaluated. We identified 68,974 cells pre-treatment and 58,852 post-treatment, with dermal cells comprising ~71% and ~66%, respectively. Supervised image analysis was performed using Visiopharm® Phenoplex™. Malignant $CD4^+$ T cells showed broad downregulation of CD27, CD103, CD25, and ICOS compared with non-malignant $CD4^+$ T cells. Malignant cells predominated at baseline and declined alongside non-malignant $CD4^+$ T cells post-treatment. At baseline, MF lesions were enriched for IL-13^+ and $CD103^+$ malignant T cells, whereas SS lesions showed higher proportions of $CD27^+$ and LAG-3^+ cells. Post-treatment, IL-13^+ malignant T cells declined, particularly in MF. Myeloid profiles differed by disease subtype and clinical response. MF lesions demonstrated baseline enrichment of M1-like macrophages ($CD86^+$, $HLA\text{-}DR^+$), whereas SS lesions were predominantly M2-polarized ($CD163^+$, $CD206^+$). Post-treatment, responders exhibited increased M1-like macrophages and preserved M1:M2 ratios, while non-responders displayed reduced M1 features. $CD11c^+$ dendritic cells were infrequent and differed in composition, with $CD14^+CD11c^+$ cells expanding in non-responders post-treatment.

Conclusion: We generated a single-cell spatial atlas of MF/SS lesions, revealing shared yet subtype-specific immune features. Distinct Th2-associated malignant T-cell profiles and myeloid organization were associated with clinical response, highlighting spatial immune signatures with potential utility for biomarker development and patient stratification in mogamulizumab therapy.

Learning Objectives:

1. Recognize MF and SS-specific malignant T-cell phenotypes and summarize treatment-associated changes during mogamulizumab therapy.
2. Identify myeloid immune features associated with clinical response, including macrophage polarization and $CD11c^+$ dendritic cell subset composition.

QUALITY OF LIFE / PATIENT REPORTED OUTCOMES

P28 Quality-of-Life and Supportive-Care Interventions in Mycosis Fungoides and Sézary Syndrome: a Scoping Review

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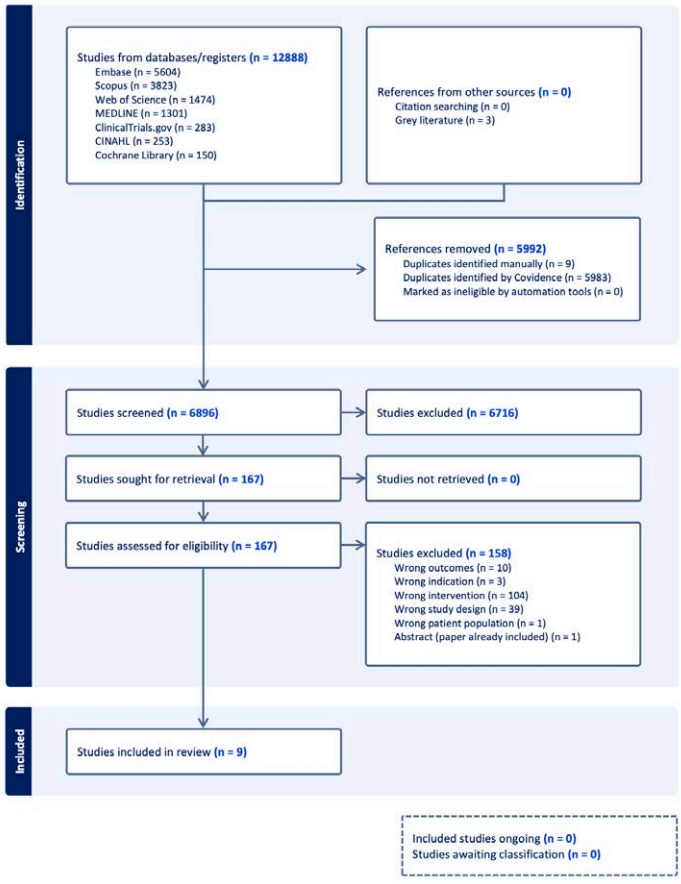
Introduction: Mycosis fungoides (MF) and Sézary syndrome (SS) are chronic cutaneous T-cell lymphomas associated with substantial symptom burden, impaired quality of life (QoL), and psychosocial distress. While disease-directed therapies increasingly report QoL outcomes as secondary endpoints, the extent, scope, and quality of evidence supporting structured supportive-care and QoL-focused interventions remain unclear. This scoping review aimed to systematically map existing interventional literature addressing QoL and supportive care in MF/SS and identify priority gaps to inform future patient-centered intervention development.

Methods, Results: A comprehensive search strategy incorporating symptom-based, psychosocial, QoL, and supportive-care terminology was executed across eight databases (MEDLINE, Embase, Scopus, Web of Science, ClinicalTrials.gov, CINAHL, and the Cochrane Library). The search yielded 12,888 records, with 5,992 duplicates removed. A total of 6,896 titles and abstracts were screened in Covidence. Eligible studies enrolled ≥10 adults with MF/SS and evaluated an interventional approach with relevance to supportive care or QoL. Full-text review identified 9 studies meeting inclusion criteria.

Of the 9 included studies, 3 evaluated antipruritic therapies, primarily aprepitant, and demonstrated improvement in pruritus using validated or numerical measures including the Dermatology Life Quality Index (DLQI), Visual Analog Scale (VAS), and numeric rating scales (NRS). One study assessed staphylococcal decolonization and reported clinical improvement without validated QoL instruments. Another evaluated radiotherapy-associated microbiome changes, similarly without formal QoL assessment. Only one study examined an educational supportive-care intervention and employed validated multidimensional QoL tools, including Skindex-29, FACT-G7, and the Illness Perception Questionnaire-Revised (IPQ-R). No studies addressed mental health interventions, psychosocial support, caregiver burden, sexual health, wound-care-specific QoL, fatigue, sleep, infection-related QoL, or resource navigation. Overall, QoL measurement was inconsistent and largely symptom-focused.



Conclusion: Despite extensive QoL burden characterization, interventional studies targeting supportive care remain scarce. Major gaps persist across psychosocial, behavioral, and practical domains of care. This highlights critical need for rigorous, evidence-based, and patient-centered supportive-care interventions in MF/SS

Learning Objectives:

1. Describe the current landscape of QoL and supportive-care interventions in MF/SS.
2. Identify supportive-care domains with limited or no interventional evidence.
3. Apply scoping-review findings to guide future patient-centered intervention development.

P29 Abstract Withdrawn

P30 Content Validity of Itch Patient-Reported Outcome Measures in Cutaneous T-Cell Lymphoma: A COSMIN-guided Qualitative Study

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Introduction: Commonly used patient-reported outcome measures (PROMs) assessing itch have not been assessed for content validity in patients with Mycosis Fungoides or Sézary Syndrome (MF/SS). We evaluated Numeric Rating Scale-Itch (NRS-Itch), Visual Analogue Scale-Itch (VAS-Itch), and Itchy Quality of Life (ItchyQoL) using COSMIN criteria[1].

Methods, Results: Semi-structured interviews were performed with 19 MF/SS patients and 9 expert clinicians. Patients completed the itch PROMs, and patients and clinicians evaluated relevance, comprehensibility, and comprehensiveness of the instruments. We assigned item-level binary ratings and conducted thematic analysis.

For itch intensity, the NRS *worst*-itch item had the highest overall rating (95% relevant, 89% comprehensible by patients, relevant by 100% of clinicians) (Table 1). NRS *average*-itch items had lower comprehensibility due to difficulty conceptualizing an average for fluctuating itch and difficulty discriminating from worst itch. VAS items had lower comprehensibility, with reproducibility and feasibility concerns. Participants frequently considered a 24-hour recall period insufficient for variability and worst flares. For ItchyQoL, three items were deemed relevant *and* comprehensible by 100% of patients (scratching, sleep, anger). The lowest patient relevance was money spent on treatments (68%) due to insurance-mitigated costs, and lowest comprehensibility was scarring (63%) due to construct ambiguity. Clinicians had lower relevance ratings, citing attribution and construct overlap in the stem "itchy skin condition" that conflated pruritus with underlying skin disease. No single instrument was fully comprehensive; 27 missing itch concepts were identified.

Table 1. Item-level content validity ratings for VAS-itch, NRS-itch, and ItchyQoL in Mycosis Fungoides/Sézary Syndrome (MF/SS). This table presents item-level binary ratings on relevance and comprehensibility for MF/SS patients (N=19), and relevance for expert clinicians (N=9).

Instrument	Item #	Concept	Patient Relevance (N=19)	Provider Relevance (N=9)	Patient Comprehensibility (N=19)
VAS	1	Average	89%	44%	58%
VAS	2	Worst	95%	44%	58%
NRS	1	Average	74%	78%	79%
NRS	2	Worst	95%	100%	89%
IQ - Symptom	1	Bleeds	100%	44%	84%
IQ - Symptom	2	Hurts	100%	78%	96%
IQ - Symptom	3	Burns/Stings	89%	89%	79%
IQ - Symptom	4	Scars	89%	44%	63%
IQ - Symptom	5	Scratching	100%	89%	100%
IQ - Symptom	6	Temperature/Season	84%	78%	95%
IQ - Function	7	Money treating	68%	67%	100%
IQ - Function	8	Work/Enjoyment	95%	89%	100%
IQ - Function	9	Interactions	95%	78%	100%
IQ - Function	10	Sleep	100%	89%	100%
IQ - Function	11	Concentration	89%	89%	100%
IQ - Function	12	Clothes	95%	89%	100%
IQ - Function	13	Buy special products	89%	78%	89%
IQ - Emotion	14	Frustrated	95%	78%	100%
IQ - Emotion	15	Embarrassed	100%	67%	89%
IQ - Emotion	16	Crazy/Nuts	100%	67%	95%
IQ - Emotion	17	Angry/Irritable	100%	89%	100%
IQ - Emotion	18	Depressed/Sad	95%	89%	100%
IQ - Emotion	19	Worry about others	89%	89%	100%
IQ - Emotion	20	Worry about itch	89%	44%	95%
IQ - Emotion	21	Self-Consciousness	89%	67%	95%
IQ - Emotion	22	Personality	84%	56%	79%

Abbreviations: VAS = Visual Analogue Scale for Itch; NRS = Numeric Rating Scale for Itch; IQ – Symptom = ItchyQoL, symptom domain; IQ – Function = ItchyQoL, function domain; IQ – Emotion ItchyQoL, emotion domain

Conclusion: The NRS *worst*-itch item showed the strongest support from patients and clinicians. ItchyQoL captured key impacts but had item-level limitations and lower clinician endorsement related to attribution and construct overlap. No instrument was fully comprehensive, suggesting a need for refinement or tailored selection for MF/SS and context of use.

References

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Learning Objectives:

1. To evaluate the content validity (relevance, comprehensibility, comprehensiveness) of the Numeric Rating Scale-Itch (NRS-Itch), Visual Analogue Scale-Itch (VAS-Itch), and the Itchy Quality of Life Questionnaire (ItchyQoL) in patients with Mycosis Fungoides and Sézary Syndrome.

P31 Overcoming Barriers to Bathing Care for Patients with Cutaneous Lymphoma: Observations from 25 Years of Nursing Care in an Australian Quaternary Referral Centre

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Introduction: Skin care and bathing strategies are an integral part of the lives of patients with cutaneous lymphoma, used both for symptom control and disease management and being common to all stages of the disease journey. Challenges in accessing and undertaking optimal bathing regimens may potentially impact on infective risk, disease and symptom management, and even dressing care. Herein, challenges and potential alternative strategies to facilitate bathing care in cutaneous lymphoma patients are explored, from over 25 years of direct nursing experience working with this patient group.

Methods, Results: Regular bathing is a cornerstone of management for cutaneous lymphoma management for symptom control as well as providing a mechanism to debulk skin bacterial load, thereby minimising the risk of disease flares or infection. The impact of infection on Cutaneous Lymphoma is known (Lindhal, et al, 2019). Bathing as well as skin care plays a crucial role in the management of Cutaneous Lymphoma (Akilov 2019).

Global assessment of the patient's independence levels, time constraints, bathing feasibility, and awareness of patient's self-care limitations are key.

Safety around bathing is critical when dealing with a less physically able patient population. Availability of able-bodied carers cannot be assumed.

Access to a bath, shower or running clean water may not be uniform among all patients with cutaneous lymphoma, with different sources of water including town water or tank water. Factors affecting water access include, geographical location, financial burden, and water shortages.

Strategies to overcome bathing challenges focus on harm minimisation, alternative bathing regimens, and optimising analgesia. Alternatives to showering may include washes by water bucket, garden watering can or reusable spray bottle.

Conclusion: Awareness of bathing challenges for patients is pivotal in optimising multimodal cutaneous lymphoma management, with the potential to significantly impact on patient symptom burden and lived experience.

Learning Objectives:

- To provide an understanding of bathing challenges patients may face when they have a diagnosis of Cutaneous Lymphoma.
- To provide practical strategies for managing bathing challenges.

P32 Health-Related Quality of Life in Cutaneous T-Cell Lymphoma Treated With Multimodality Therapy Including Extracorporeal Photopheresis: A Latin American Experience

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Introduction: Cutaneous T-cell lymphomas (CTCL), including mycosis fungoides (MF) and Sézary syndrome (SS), significantly impair health-related quality of life (HRQOL) due to chronic skin symptoms, pruritus, and psychosocial burden. Although extracorporeal photopheresis (ECP) is a cornerstone therapy for advanced CTCL, data evaluating its impact on HRQOL are limited, and no previous studies from Latin America have specifically addressed patient-reported outcomes in this setting.

Methods, Results: A retrospective descriptive cohort study was conducted including patients with histopathologically confirmed CTCL treated at Hospital Italiano de Buenos Aires between July 2011 and February 2024. All patients received ECP for a minimum of three months in combination with at least one additional biologic response modifier. ECP was administered in 2-day cycles every 2–4 weeks using the Therakos system. Clinical data were collected from medical records. HRQOL was assessed using the validated Skindex-29 questionnaire at baseline and every six months during treatment.

Twenty-eight patients were included (median age 63 years). Eleven patients had MF (39%) and seventeen SS (61%). Median number of prior treatments was 2, and median number of concomitant therapies during ECP was 3. Baseline Skindex-29 scores demonstrated impairment across all domains, with the highest burden in the symptoms domain (mean score 50), followed by emotions (30) and functioning (25). Patients with SS exhibited particularly high symptom scores. The most frequently affected items included pruritus, skin sensitivity, emotional distress related to disease progression, social interaction difficulties, and impaired sexual life. Clinically meaningful improvement after treatment was observed primarily in the symptom domain.

Conclusion: This study represents the first Latin American report evaluating HRQOL in CTCL patients treated with multimodality therapy including ECP. Symptom burden was the most affected HRQOL dimension and showed clinically relevant improvement with treatment. These findings provide a foundation for future prospective longitudinal studies integrating patient-reported outcomes in CTCL.

Learning Objectives:

1. Understand the multidimensional impact of CTCL on patient-reported quality of life, emphasizing symptoms, emotional burden, and functioning.
2. Recognize the role of multimodality therapy including ECP in modifying HRQOL outcomes.
3. Appreciate the significance of region-specific data in CTCL HRQOL research and identify knowledge gaps for future studies.

P33 Quality of Life in Cutaneous T-Cell Lymphoma: Current Insights and Future Directions

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Introduction: Cutaneous T-cell lymphoma (CTCL) is a chronic and heterogeneous skin lymphoma. CTCL manifests through a range of skin symptoms, including patches, plaques, tumors and erythroderma, which can cause itch, pain, and discomfort. These physical symptoms often lead to sleep disturbances, fatigue, and limitations in daily life activities. The symptom burden and long-term disease control strongly influence quality of life (QoL). In recent years, assessment of QoL has developed into an important, indispensable, outcome measure. Whereas in prior clinical trials classical outcome measures such as survival or formal treatment responses where measured, integration of QoL assessments have become more

and more important. Despite the increasing attention that is paid to patient-reported outcomes in CTCL, there are many remaining challenges.

Methods, Results: A growing body of quantitative and qualitative research has examined quality of life in CTCL. Findings from validated questionnaires, complemented by data from open and semi-structured patient interviews, have been consolidated to provide a comprehensive overview of patient-reported experiences. Across studies, quality of life impairment is consistently reported, with pruritus, visible skin changes, fatigue, and treatment burden identified as key contributors. Importantly, qualitative data highlight aspects insufficiently captured by questionnaires alone, including emotional distress, social stigma, and uncertainty related to the chronic nature of the disease. This narrative review provides new insights on the clinical implementation of quality of life integration in the care of CTCL patients.

Conclusion: Improving quality of life in CTCL requires systematic assessment of patient-reported outcomes, better symptom-directed therapies, and incorporation of quality-of-life endpoints in future research and clinical practice. A patient-centered approach is essential to guide treatment decisions and optimize long-term care to better align treatment strategies with patient priorities.

Learning Objectives:

Understanding the importance of quality of life

P34 Evaluation of an Educational Video to Support Understanding of Health-Related Quality of Life for Patients with Cutaneous T-Cell Lymphoma

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Introduction: Cutaneous T-cell lymphoma (CTCL) is a group of non-Hodgkin lymphomas that significantly affects health-related quality of life (HRQoL). We aim to develop a core domain set (CDS) for HRQoL in CTCL using multi-round Delphi surveys, requiring participants to understand complex concepts that could potentially limit meaningful patient engagement. We evaluated whether a brief patient-directed educational video improved comprehension of concepts related to clinical research and HRQoL.

Methods, Results: Patient/caregiver participants invited to an ongoing electronic Delphi (e-Delphi) survey study completed a baseline assessment of knowledge of clinical trials, HRQoL, core domain sets, and Delphi exercises. Participants were then offered viewing of an optional [<4 minutes long] educational video. A post exposure quiz was presented to all participants. Video viewers rated informativeness, engagement, clarity, and usefulness on five-point Likert scales. Knowledge change was calculated as the post-quiz minus baseline quiz score and compared between video viewers and non-viewers using Mann–Whitney U tests ($p<0.05$). Fifty-three patients/caregivers completed the pre- and post-exposure quizzes, and 31 viewed the video. Participants overall demonstrated high baseline understanding of clinical trials and Delphi methodology (Table 1). Among video viewers, the greatest improvement was for the core domain set item (90.3% to 96.8%). There was no difference in overall knowledge change between video viewers and non-viewers (median $\Delta = 0$ vs 0; Mann–Whitney $U = 337.5$, $p = 0.95$). Video acceptability was high: 96.8% of participants rated clarity, informativeness, and usefulness positively, and 93.5% reported high engagement.

Item	No video viewed (N=22)	Video viewed (N=31)		
	Baseline % correct	Post-quiz % correct	Baseline % correct	Post-quiz % correct
Q1 Clinical Trial	100% (22/22)	100% (22/22)	96.8% (30/31)	100% (31/31)
Q2 HrQOL	86.4% (19/22)	95.5% (21/22)	93.5% (29/31)	90.3% (28/31)
Q3 Core Set	90.9% (20/22)	90.9% (20/22)	90.3% (28/31)	96.8% (30/31)
Q4 Delphi	100 (22/22)	95.5% (21/22)	100% (31/31)	96.8% (30/31)

Conclusion: We present a scalable approach to supporting patient understanding. While there was high baseline understanding, the educational video was highly accepted by patients. Similar interventions may support participant engagement and help ensure research reliant of patient reported data reflects better informed patient perspectives.

Learning Objectives:

1. To assess the impact of a brief educational video on patient understanding of health-related quality of life concepts.
2. To apply multimedia educational strategies to enhance patient-informed consensus building in clinical trials for rare diseases such as cutaneous T-cell lymphoma.

THERAPEUTICS / PRECLINICAL STUDIES

P35 Treatment Outcomes and Recurrence Patterns Following Local Therapies in Primary Cutaneous Marginal Zone and Follicle Center Lymphoma

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Introduction: Primary cutaneous marginal zone lymphoma (PCMZL) and primary cutaneous follicle center lymphoma (PCFCL) are indolent B-cell lymphomas typically managed with skin-directed therapies. Radiation therapy (RT) is a well-established standard treatment, while intralesional kenalog (ILK) and excision are low-toxicity alternatives for localized disease. Real-world data comparing treatment durability and recurrence patterns remain limited.

Methods, Results: A retrospective, single-center study was conducted of n=20 patients with PCMZL (n=12) and PCFCL (n=8), comprising 25 treated lesions Patients were categorized into treatment cohorts based on their initial localized therapy modality:

RT, surgical excision, ILK. Endpoints included initial clinical response, time to recurrence (TTR), recurrence location (local vs. distant), and treatment-related toxicity.

Of the 25 lesions analyzed, 15 (60%) were treated with RT, 8 (32%) with surgical excision, and 2 (8%) with ILK. Initial complete response rates were high for excision (n=8/8, 100%) and RT (n=14/15, 93.3%). ILK was associated with incomplete response in this limited cohort (n=2, 0% CR). While the patient-level recurrence rate was 55% (n=11/20), local control remained durable; 86.7% (n=13/15) of RT-treated sites and 87.5% (n=7/8) of excised sites remained clear of disease. Among patients who experienced recurrence, 63.6% (n=7/11) developed disease at new anatomical sites. Median TTR was the longest following excision (40.5 months), compared with RT (14.0 months) and ILK (14.0 months). No systemic toxicities were observed.

Conclusion: Localized skin-directed therapies achieve high initial clearance in PCBCL, but recurrence, predominantly at distant sites, is common, emphasizing the chronic, multifocal nature of disease. RT and excision provide durable local control, while ILK may serve as a radiation-sparing option for selected patients with multifocal disease. This study is limited by its retrospective single-center design, small sample size, and limited power to compare treatment modalities.

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Learning Objectives:

1. Describe real-world treatment outcomes of radiation therapy, intralesional corticosteroids, and excision in patients with primary cutaneous B-cell lymphomas.
2. Compare response rates, recurrence patterns, and toxicity associated with local radiation therapy, excision, and intralesional corticosteroid treatment in primary cutaneous B-cell lymphomas.

P36 Comprehensive Characterization of DT-7012, a Highly Differentiated Anti-CCR8 Depleting Antibody in CTCL

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Introduction: CCR8 has recently emerged as a promising target in the treatment of cutaneous T cell lymphoma. DT-7012 is a differentiated humanized anti-CCR8 IgG1 monoclonal antibody engineered for optimized binding and enhanced effector functions to deplete CCR8+ tumor cells in CTCL cells, as well as CCR8^{+} tumor-resident Tregs, while maintaining peripheral immune integrity.

The objective of this study was to evaluate the expression of CCR8 in CTCL, and to complete the preclinical characterization of DT-7012, focusing on its binding properties, effector-function potencies, and potential activity in CTCL.

Methods, Results: CCR8 and FoxP3 expression were analyzed by immunohistochemistry on CTCL cutaneous biopsies. Comprehensive *in vitro* assays were performed to assess DT-7012 binding in presence of its ligand CCL1. Functional activity was evaluated through antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP) assays using CTCL tumor models and tumor activated Treg models.

CCR8 is expressed in different subtypes of CTCL by both tumor cells and Treg cells, with a statistically significant difference in the percentage of CCR8-positive tumor cells among the different lymphoma subtypes.

In cell-based assays, DT-7012 shows binding in the presence of its ligand CCL1, and DT-7012 induced potent cytotoxicity and phagocytosis in both patient derived CTCL models and tumor activated Tregs models. Collectively, these findings support DT-7012 as a promising CCR8 drug candidate for the treatment of CTCL patients.

Conclusion: DT-7012 emerges as a promising therapeutic antibody in CTCL with a dual mechanism of action, targeting both tumor cells and the immunosuppressive Treg microenvironment. These results provide a preclinical rationale for clinical evaluation in CTCL patients. DT-7012 is entering clinical evaluation as it obtained authorization for the Phase 1, multicenter, open-label, first-in-human dose-escalation study in patients with relapsed or refractory CTCL (CITY; NCT07213882).

Learning Objectives:

- Understand the role of CCR8 in CTCL and its relevance as a therapeutic target.
- Describe the preclinical characteristics and mechanism of action of an anti-CCR8 antibody, DT-7012, in CTCL.

P37 Post Hoc Analysis of a Randomized, Controlled, Phase 2 Study to Assess the Efficacy of Chlormethine Gel in Patients with Early-stage Mycosis Fungoides Based on Skin Phototype

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Introduction: Phototherapy and topical chlormethine are first-line skin-directed treatment options for mycosis fungoides (MF). Therapeutic efficacy of phototherapy can vary by skin phototype, particularly if initial dosing and up-titration are inadequate. However, whether skin phototype influences the efficacy of chlormethine gel remains unclear. In this post hoc analysis, we evaluated the efficacy of chlormethine gel in different skin phototypes in a phase 2 randomized, controlled trial (NCT00168064) in which chlormethine gel was found to be noninferior to equal strength chlormethine ointment.

Methods, Results: Patients who received chlormethine gel (0.016%) for 12 months during the study were included. Response was assessed using the Composite Assessment of Index Lesion Severity (CAILS) score. Response rates (≥50% improvement from baseline) and changes from baseline in CAILS scores in intent-to-treat [ITT], efficacy

evaluable [EE] and completer populations were compared between patients with dark and light skin at each visit by logistic regression and ANCOVA, respectively. Disease stage (IA, IB/IIA) was used as a stratification factor.

Demographics for the 129 included patients are shown in Table 1. No statistically significant differences in CAILS response rates or change in CAILS scores from baseline were observed between patients with dark and light skin for any visit across the ITT, EE and Completer populations. Specifically, in patients with dark and light skin in the ITT population, CAILS response rates at 12 months were 57.5% and 50.3%, respectively (odds ratio: 1.34; p=0.48) and changes in CAILS scores from baseline were -20.93 and -19.36 (least-squared mean difference: -1.57; p=0.65).

Table 1. Baseline demographics

Variable	Patients with dark skin (n/N)	Patients with light skin (n/N)	All Patients (n/N)
Gender			
Female	42.4 (14/33)	40.6 (39/96)	41.1 (53/129)
Male	57.6 (19/33)	59.4 (57/96)	58.9 (76/129)
Age category			
18 to 64	78.8 (26/33)	68.8 (66/96)	71.3 (92/129)
65 to 74	18.2 (6/33)	24 (23/96)	22.5 (29/129)
≥ 75	3 (1/33)	7.3 (7/96)	6.2 (8/129)
Mycosis fungoides stage at baseline			
Strata 1 - Stage IA	45.5 (15/33)	62.5 (60/96)	58.1 (75/129)
Strata 2 - Stage IB or 2A	54.5 (18/33)	37.5 (36/96)	41.9 (54/129)
Efficacy evaluable population	78.8 (26/33)	66.7 (64/96)	69.8 (90/129)
Completers population	66.7 (22/33)	61.5 (59/96)	62.8 (81/129)

ITT: all randomized patients

Efficacy evaluable: a subset of the intent-to-treat population with at least 6 months continuous treatment

Completers: a subset of the ITT population with continuous treatment for the entire study

Conclusion: This post hoc analysis suggests that chlormethine gel is equally effective across a range of skin phototypes, with no statistically significant differences in response rates or CAILS score improvement after 12 months of therapy. Further prospective studies are warranted to review these findings across diverse patient populations.

Learning Objectives:

To describe that chlormethine gel demonstrates equivalent efficacy in MF patients with dark and light skin, as measured by changes in CAILS scores over multiple visits in an intent-to-treat population.

P38 EORTC 1820-MOGAT – Mogamulizumab Plus Total Skin Electron Beam Therapy in Patients with stage IB-IIB Cutaneous T-Cell Lymphoma

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Introduction: Cutaneous T-cell lymphomas (CTCL) are rare non-Hodgkin lymphomas, with mycosis fungoides (MF) accounting for ~60% of cases. MF is radiosensitive, making total skin electron beam therapy (TSEB) a key treatment for early-stage disease. While TSEB achieves high response rates (up to 87%), responses are short-lived (median 11.8 months). Mogamulizumab, an anti-CCR4 antibody, is approved for MF and Sézary syndrome (SS) and is particularly effective in blood, whereas TSEB is highly effective for skin lesions. Combining these modalities may improve outcomes. Lower-dose TSEB offers similar efficacy with reduced toxicity.

We hypothesize that sequential treatment with mogamulizumab and low-dose TSEB will improve progression-free survival at 48 weeks (PFSR-48) compared to historical outcomes with either treatment alone.

Methods, Results: MOGAT (NCT04128072) is a multicenter, international, open-label, single-arm phase II trial. Eligible patients have MF stage IB–IIB and have failed at least one prior systemic therapy. Treatment consists of two cycles of mogamulizumab, followed by TSEB (12 Gy in eight fractions over two weeks) while mogamulizumab is paused, then resuming mogamulizumab for up to 18 months. The primary endpoint is PFSR-48 per EORTC-ISCL-USCLC criteria. The study aims to detect a 20% improvement in PFSR-48 using an Ahern design (type I and II errors fixed at 10%). Thirty-nine evaluable patients are required. Secondary endpoints include safety, overall survival, time to progression, duration of response, and time to next treatment. Quality of life and translational research are exploratory endpoints.

Trial Status: First patient enrolled March 2023; 14 European sites active. As of January 5, 2026, recruitment is nearly complete, with 44 patients enrolled, 2 in screening, and 35 evaluable (90% of target).

Conclusion: MOGAT explores an innovative approach combining mogamulizumab before and after TSEB for systemic and skin disease control. If successful, confirmatory studies are warranted

Learning Objectives:

Security and efficacy of a new treatment combination for mycosis fungoides stages IB-IIB

P39 Use of Immune Checkpoint Inhibitors in Refractory Mycosis Fungoides and Sézary Syndrome: a Systematic Review

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Introduction: Cutaneous T-cell lymphomas (CTCLs) are defined by malignant monoclonal T-cell infiltration of the skin. Mycosis fungoides (MF) and Sézary syndrome (SS) account for approximately 50% of CTCLs, with MF presenting as pruritic patches or plaques and SS characterized by erythroderma, blood involvement, and lymphadenopathy. Current therapies are largely palliative, progressing from skin-directed treatments to systemic and biologic agents. Immune checkpoint inhibitors (ICIs) have emerged as potential options in refractory disease. This systematic review evaluates the efficacy and safety of ICIs in MF/SS.

Methods, Results: A systematic search of MEDLINE, Embase, and Cochrane databases was conducted according to PRISMA guidelines and PROSPERO registration (CRD42024570032). Twenty-two studies published between 2014 and 2024 were included, encompassing 66 patients with refractory MF/SS. Study quality was assessed using the Oxford Centre for Evidence-Based Medicine Levels of Evidence.

Treatment outcomes were available for 60 patients, most receiving ICI monotherapy (85%). Pembrolizumab was the most frequently

used agent, followed by nivolumab, ipilimumab, and atezolizumab. Overall responses included complete response (CR) in 20%, partial response in 33.3%, stable disease in 31.7%, and progressive disease in 16.7%. Pembrolizumab accounted for 66.7% of CRs. Mean treatment duration was 33 weeks. Treatment-limiting adverse events occurred in 8.3% of cases, with no treatment-related deaths reported.

Conclusion: ICI therapy, particularly PD-1/PD-L1 blockade with pembrolizumab, demonstrates meaningful clinical activity in refractory MF/SS with an acceptable safety profile. However, targeting this axis may have dual effects on benign and malignant T cells, underscoring the need for careful patient selection. Tumor molecular profiling may help identify patients most likely to benefit. Larger, prospective randomized trials are needed to define efficacy, safety, and optimal patient selection.

Learning Objectives:

- Describe the efficacy and safety profile of immune checkpoint inhibitors in refractory MF and SS.
- Understand the biological rationale and risks of targeting the PD-1/PD-L1 axis in CTCL.
- Recognize the importance of molecular profiling in selecting CTCL patients for ICI therapy.

P40 Real-Life Efficacy of Immunotherapy for Sézary Syndrome: a Multicenter Observational Study

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Introduction: Sézary syndrome (SS) is a rare and aggressive cutaneous T-cell lymphoma. Mogamulizumab, a CCR4-targeting monoclonal antibody, has shown benefits in progression-free survival in clinical trials for CTCL. This study evaluated overall survival (OS) and prognostic factors in SS, including the impact of mogamulizumab, in a real-life setting.

Methods, Results: Data were gathered retrospectively from 24 centers in Europe for patients diagnosed between 2000 and 2020 with Sézary syndrome (stage IV, ISCL/EORTC) or pre-Sézary syndrome (stage IIIB). A multivariable Cox proportional hazard ratio model analyzed: age, disease stage, plasma lactate dehydrogenases levels, blood eosinophilia at diagnosis, large-cell transformation and treatment received. Time to Next Treatment (TTNT) was performed on all treatment types. This study is registered in ClinicalTrials (SURPASSe01 study: NCT05206045).

Among 339 patients (58% men, median age at diagnosis 70 years, Q1-Q3, 61–79): 33 (9.7%) had stage IIIB, 296 (87.3%) had stage IV and 10 (2.9%) had large-cell transformation. A total of 110 patients received mogamulizumab. Median follow-up was 58 months (95% confidence interval (CI), 53–68), and 5-year OS was 46.5% (95% CI, 40.6–53.3). Independent predictors of worse OS were age ≥80 versus 50 (HR 4.9, 95% CI 2.1–11.2, p=0.001) and large-cell transformation (HR 2.8, 95% CI 1.6–5.1, p=0.001). Mogamulizumab treatment was significantly associated with increased OS (HR 0.34, 95% CI 0.15–0.80, p=0.013). Mogamulizumab treatment, extracorporeal photopheresis (ECP), and allogeneic hematopoietic stem cell transplant (alloHSCT) were associated with significantly higher TTNT in multivariable analysis (Table 1).

Summary of time to next treatment analyses.

Variable	Median TTNT (months) [95% CI]	Univariable HR [95%CI]	p.value	Multivariable HR [95%CI]	p.value
Not treated with ECP	6 [5 ; 7]				
Treated with ECP	17 [13 ; 20]	0.77 [0.66 ; 0.88]	0.001	0.78 [0.64; 0.95]	0.013
Not treated with MTX	6 [5 ; 8]				
Treated with MTX	13 [10; 17]	0.78 [0.68; 0.90]	0.001	0.94 [0.77; 1.15]	0.54

Not treated with alloHSCT Treated with alloHSCT	8 [7; 9] 41 [36; NA]	0.33 [0.16; 0.71]	0.004	0.26 [0.10; 0.66]	0.005
Not treated with interferon Treated with interferon	7 [6; 9] 13 [8; 20]	1.21 [1.03; 1.41]	0.02	1.42 [1.12; 1.79]	0.004
Not treated with mogamulizumab Treated with mogamulizumab	7.5 [7; 9] 24 [19; 28]	0.87 [0.68; 1.10]	0.24	0.51 [0.35; 0.73]	<0.001
Not treated with monochemotherapy Treated with monochemotherapy	8 [7; 10] 7 [5.5; 10]	2.23 [1.91; 2.60]	<0.0001	1.40 [1.09; 1.81]	0.008
Not treated with polychemotherapy Treated with polychemotherapy	8 [7; 10] 6 [3; 10]	2.51 [2.02; 3.13]	<0.0001	1.44 [0.99; 2.08]	0.055

Conclusion: Mogamulizumab therapy was significantly and independently associated with decreased mortality in Sézary syndrome.

Learning Objectives:

- The epidemiology of a large cohort of patients with Sézary syndrome.
- Mogamulizumab treatment was significantly associated with increased overall survival (OS) and significantly higher time-to-next treatment (TTNT) in multivariable analysis.

P41 Mogamulizumab: Real-World Experience in Heavily Treated Patients With Mycosis Fungoides and Sézary Syndrome: Durable Efficacy and Tolerability

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Introduction: Cutaneous T-cell lymphomas (CTCL), including mycosis fungoides (MF) and Sézary syndrome (SS), are chronic, relapsing malignancies with limited treatment options in advanced stages. Although mogamulizumab has demonstrated efficacy in clinical trials, real-world data remain limited. This study aimed to evaluate the real-world efficacy, durability of response, and safety of mogamulizumab in heavily treated patients at a single center.

Methods, Results: We performed a retrospective analysis of patients with advanced, relapsed or refractory MF or SS treated with mogamulizumab. Best overall response was assessed by physician evaluation and supported by compartment-specific responses in the skin, blood, and lymph nodes. Outcomes included overall response rate (ORR), progression-free survival (PFS), duration of response (DOR) and overall survival (OS). Safety outcomes included treatment-emergent adverse events and treatment discontinuation.

Results: Ten patients with advanced CTCL were included (median age 72 years; range, 40–78), having received 2–6 prior systemic therapies. Among nine evaluable patients, ORR was 78%, driven by cutaneous improvement, including skin clearance in 7/9 and resolution of erythroderma in 5/8. Following mogamulizumab administration, rash occurred in 4/10 patients: 1 experienced a severe immediate infusion reaction requiring epinephrine, while the remaining 3 were managed conservatively. Median PFS was 23 months (range, 10–51). Responses were durable, with several lasting ≥1 year, including some >2 years. OS was assessed descriptively; one non–treatment-related death occurred during follow-up (up to 48 months). Treatment-emergent adverse events occurred in 80% of patients, most commonly hematologic, leading to discontinuation in 2/10.

Conclusion: In routine clinical practice, mogamulizumab demonstrated durable, clinically meaningful benefit in a subset of patients with advanced MF or SS, supporting its role as an effective and well-tolerated option that may reduce the need for more toxic systemic therapies, particularly in older, heavily treated patients.

Learning Objectives:

1. Summarize real-world treatment outcomes of mogamulizumab in advanced mycosis fungoides and Sézary syndrome.
2. Identify key safety considerations when using mogamulizumab in older, heavily treated patients.

P42 A Phase 1, Multicenter, Prospective, First-In-Human Dose-escalation Clinical Trial of anti-CCR8 Monoclonal Antibody DT-7012 in Patients with Relapsed or Refractory CTCL

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Introduction: CCR8 is a surface marker of tumor-infiltrating regulatory T cells. We have recently observed that CCR8 was expressed by tumor cells in CTCL and other peripheral T-cell lymphomas. CCR8 is expressed by skin resident-memory T cells which are believed to be the tumor cell-of-origin in mycosis fungoides. Kainova Therapeutics showed the in vitro efficacy of their proprietary anti-CCR8 mAb DT-7012 in the depletion of CTCL cells. Therapeutic depletion of CCR8-expressing cells by DT-7012 could eliminate tumor cells and activate the anti-tumor immunity in CTCL.

We hypothesize that treatment with DT-7012 is effective in relapsing or refractory (R/R) CTCL as advanced MF and SS.

Methods, Results: CITY is a single arm, open-label, multicenter prospective phase 1 dose-escalation study using the time-to-event continual reassessment method design.

We will include 30 adult patients with CTCL (MF and SS), stage IB or higher, relapsing or refractory after at least two lines of systemic treatments, in the dermatology departments of 4 university hospital

centers in France and Spain (first centers scheduled to open in May 2026).

The Primary objective is to identify the maximum tolerated dose (MTD) of intravenous dosing of single agent DT-7012, in terms of short-term safety & tolerability.

Secondary objectives are to assess DT-7012 safety (adverse events), efficacy(response), pharmacokinetics, the immunogenicity of DT-7012, DT-7012 effect on pruritus (patient reported outcome), health-related quality of life (patient reported outcome), Time To Next Treatment, disease control rate (DCR: ORR + stable disease), duration of response, progression-free survival (PFS).

Conclusion: We expect a higher disease control of the lymphoma in the participants, compared to standard of care, with a favorable safety profile. As such, we expect an improved quality of life in participants. We also expect a better understanding of the disease pathophysiology.

Learning Objectives:

After viewing this presentation, participants will be aware of the objectives of a new phase 1 study CITY evaluating anti-CCR8 monoclonal antibody (DT-7012) in patients with relapsed or refractory cutaneous T-cell lymphomas.

P43 BUFALLO is a Novel Reduced Intensity Conditioning Regimen for the Allogeneic Stem Cell Transplantation for Patients with Primary Cutaneous T-Cell Lymphomas

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Introduction: The survival rate of patients with advanced-stage T-cell lymphomas remains poor with a median overall survival often below 40 months. For these patients immunotherapy with allo-HCT is the only curative option.

But, major limitation of allo-SCT is the increased relapse rate which occurs in nearly 50% of the cases. Also, there is no available data supporting the use of maintenance strategies. Given the high frequency of mutations and constitutive activation of the JAK-STAT pathway in T-cell lymphomas the use of ruxolitinib seems pathogenetically justified.

Methods, Results: Four patients (three male and one female) with a median age of 50 years (45–53) were included in this study. Two patients had a diagnosis of SS, 1 – CD8+ aggressive epidermotropic T-cell lymphoma, 1 – PTCL, NOS. Patients were heavily pre-treated: the median number of lines of treatment was four (2–6). One patient had complete remission, two - partial remission, one - stable disease at the time of transplant.

A reduced intensity conditioning regimen consisting of fludarabine 150 mg/m2 and bendamustine 390 mg/m2. GVHD prophylaxis consisted of ruxolitinib 15 mg days +5 to +20, 10 mg days +21 to +90 -180 plus Mycophenolate Mofetil 30-45 mg/kg days +5 to +30 plus post-transplant cyclophosphamide 25 mg/kg days +3, +4 for MRD and MUD respectively.

Engraftment occurred in all patients at a median of 13 day after graft infusion. Full donor chimerism was achieved in all patients at first evaluation (day +30). Three of four patients with PR achieved CR (day +30). One patient developed acute GVHD. The early transplant period was complicated by bacterial infections (25%) and viral infections(75%).

Conclusion: The limitation of our study is the small number of patients and a short period of follow-up. However, the results of our study are promising and should be tested in larger number of patients.

Learning Objectives:

allogeneic stem cell transplantation, new conditioning regimen

P44 Topical JAK Inhibitors in Early-Stage Mycosis Fungoides: a Systematic Review

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Introduction: Mycosis fungoides (MF) is the most common subtype of cutaneous T-cell lymphoma (CTCL) and is typically managed with skin-directed therapies in early stages. However, many patients experience incomplete responses, recurrent disease, or treatment-limiting adverse effects, highlighting the need for additional well-tolerated topical options. Dysregulation of the Janus kinase–signal transducer and activator of transcription (JAK–STAT) pathway has been implicated in MF pathogenesis and disease progression, suggesting that topical JAK inhibitors may provide a targeted approach with limited systemic exposure.

Methods, Results: This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We will evaluate the efficacy and safety of topical JAK inhibitors for early-stage MF (stage IA–IIA). A comprehensive search of PubMed/MEDLINE, Embase, Web of Science, Scopus, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) will be performed using keywords related to MF, CTCL, and topical JAK inhibitors (including ruxolitinib, tofacitinib, and delgocitinib). Reference lists and gray literature will be manually screened. Eligible studies will include clinical trials, observational studies, case series, and case reports in human participants treated with at least one topical JAK inhibitor. Exclusion criteria include non-human studies, non-MF cutaneous lymphomas, and reports lacking extractable clinical outcomes. Results will be synthesized narratively, with clinical response and adverse events summarized across included studies.

Conclusion: This review will synthesize available evidence on topical JAK inhibitors in early-stage MF and clarify their potential role as adjunct or alternative skin-directed therapy, informing future prospective studies and clinical trial design.

Learning Objectives:

- Explain the rationale for topical Janus kinase (JAK) inhibitors in early-stage mycosis fungoides (MF).
- Summarize reported efficacy outcomes of topical JAK inhibitors in MF.
- Assess safety/tolerability and identify evidence gaps for future trials.

P45 Mogamulizumab Treatment for Mycosis Fungoides in Clinical Practice in France: Data from the Ongoing Multicentric Prospective Observational PROMED Study

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Introduction: Mogamulizumab, an anti-CCR4 defucosylated antibody, is approved for the treatment of patients with mycosis fungoides (MF) and Sézary syndrome (SS) who have received ≥1 prior systemic therapy. There is limited real-world evidence specifically focusing on MF patients with early-stage disease and low blood burden treated with mogamulizumab. Here, we present initial results from the ongoing PROMED study, investigating mogamulizumab in patients with MF in a French cohort.

Methods, Results: PROMED is an ongoing prospective, non-interventional study that recruited MF patients at 16 sites in France, with a maximum follow-up time of 18 months. Follow-up visits were planned every 3 months. Data were collected from electronic medical records, patient diaries, and patient-reported outcomes tools. Eligible patients had a histologically confirmed MF diagnosis, had been examined for blood involvement (B0, B1) and T-cell clonality (skin and blood) within 3 months prior to inclusion, and received a nodal and metastatic assessment. Patients with confirmed SS (B2 blood involvement) were excluded.

The eligible population consisted of 50 patients (median age 61.9 years; 66.0% male). At baseline, median disease duration was 3.9 years. Patient demographics are summarized in the **Table**. The majority (60.0%) of patients had stage IB disease. Initial blood staging was B0 in 43 patients (86.0%) and B1 in 7 patients (14.0%). The median number of prior systemic therapies was 2, and mogamulizumab was initiated after at least one previous systemic treatment in 47 patients (94.0%), most commonly following exposure to methotrexate and bexarotene.

Table. Baseline Patient Characteristics

	FAS Population (n=50)
Median age, years (min, max)	61.9 (31, 90)
Male sex, n (%)	33 (66)
ECOG PS, n (%)	
0	31 (62)
1	15 (30)
2	3 (6)
3	1 (2)
Clinical stage, n (%)	
Early stages	32 (64)
IA	2 (4)
IB	30 (60)
IIA	0 (0)
Advanced stages	18 (36)
IIB	6 (12)
IIIA	8 (16)
IIIB	3 (6)
IVA2	1 (2)
IVB	0 (0)
Blood staging, n (%)	
B0	43 (86)
B1	7 (14)
Large cell transformation[a], n (%)	5 (10)
Median disease duration at mogamulizumab initiation, years (min, max)	3.9 (0, 24)
Median number of prior systemic therapies, n (min, max)	2 (0, 9)
At least one previous systemic treatment, n (%)	**47 (94)**
Methotrexate, n (%)	39 (78)
Bexarotene, n (%)	29 (58)
Interferon alpha, n (%)	14 (28)
Chemotherapy, n (%)	11 (22)
Brentuximab, n (%)	7 (14)
Photopheresis, n (%)	3 (6)
Romidepsin, n (%)	1 (2)
Other systemic treatment, n (%)	11 (22)

ECOG, Eastern Cooperative Oncology Group; FAS, Full Analysis Set; MF, mycosis fungoides; max, maximum; min, minimum; PS, performance status.

[a]Large cell transformation had to be noted according to study protocol.

Conclusion: Initial results from the PROMED study describe mogamulizumab use in MF patients with a mostly early-stage disease; most had no or low blood burden at inclusion. Outcome data collection regarding efficacy and safety is ongoing. This study will provide valuable real-world insights into the use of mogamulizumab in MF patients with no or low blood burden in France.

Learning Objectives:

After viewing this presentation, participants will be aware of current real-world investigation of mogamulizumab use in patients with mycosis fungoides in France.

P46 Combination Low-dose Radiotherapy and Topical Imiquimod May Stimulate a Systemic Anti-tumor Response in Mycosis Fungoides

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Introduction: Topical imiquimod (IMQ), a toll-like receptor 7 agonist, is an effective skin-directed immunotherapy for early mycosis fungoides (MF). Preclinical data suggest that combining innate immune activation with radiotherapy (RT) may induce systemic antitumor immunity. We conducted a single-arm pilot study evaluating the safety and efficacy of combined topical IMQ and low-dose RT in MF.

Methods, Results: Fifteen patients with stage IA-IIB MF refractory to ≥1 prior therapy and ≥4 discrete MF lesions were enrolled. IMQ 5% cream was applied to designated lesions to be treated 3–5 days/week for 6 weeks. After one week, these lesions also received local RT (8 Gy/2fractions). Designated untreated lesions were followed in parallel. Clinical response was assessed at week 8 using modified Severity-Weighted Assessment Tool (mSWAT) and Composite Assessment of Index Lesion Severity (CAILS). An adjusted mSWAT excluding irradiated lesions assessed systemic effects. Paired skin biopsies from treated and untreated sites were obtained at weeks 0 and 8.

The cohort included 10 men and 5 women (mean age 59 years; IA n=4, IB n=8, IIB n=3). Unadjusted and adjusted mSWAT scores decreased from weeks 0 to 8 (means 36.5 to 16.7 and 23.7 to 13.9; p<0.001). Both treated and untreated lesions demonstrated CAILS reductions (24.6 to 10.7 and 18.9 to 15.6, respectively; p<0.05). Histologically, treated lesions showed near-complete (n = 12) or mild/moderate (n = 3) reduction of atypical lymphocytes, while untreated lesions showed near-complete reduction in 4 patients and mild/moderate reductions in 6 patients. Clinically, 7 patients achieved partial response, 6 were stable and 2 progressed, suggesting a 47% overall response rate. Adverse effects were limited to local skin irritation and pain.

Table 1: Clinical and histopathologic changes in skin severity from baseline (week 0) to post-treatment (week 8)

	Adjusted mSWAT Change (%)*	Adjusted Clinical Response †	Total mWAT Change (%)	Clinical Response	Treated CAILS Change (%)	Untreated CAILS Change (%)	Untreated Histological Response
IMQ 4	-90	PR	-84	PR	-75	-62	Near Complete
IMQ 8	-80	PR	-81	PR	-94	-12	Near Complete
IMQ 21	-79	PR	-65	PR	-67	-32	Mild/ Moderate
IMQ 11	-68	PR	-68	PR	-51	-44	Mild/ Moderate
IMQ 9	-55	PR	-63	PR	-85	-34	Minimal/ None
IMQ 5	-53	PR	-55	PR	-42	-24	Mild/ Moderate
IMQ 1	-51	PR	-66	PR	-82	-65	Near Complete
IMQ 3	-46	SD	-48	SD	-65	-19	Minimal/ None
IMQ 20	-39	SD	-42	SD	-73	-14	Mild/ Moderate
IMQ 15	-30	SD	-47	SD	-30	-33	Near Complete
IMQ 6	-26	SD	-32	SD	-72	-39	Minimal/ None
IMQ 19	0.8	SD	-11	SD	-19	-13	Minimal/ None
IMQ 14	2.5	SD	-35	SD	-74	-16	Mild/ Moderate
IMQ 12	43	PD	-53	PR	-39	-21	Mild/ Moderate
IMQ 7	281	PD	-63	PR	-76	-32	Minimal/ None

*Adjusted mSWAT (Total mSWAT excluding directly treated lesions)

†Clinical response based on skin response criteria for MF (Olsen et al, J Clin Oncol 2011)

PR = partial response (50-99% clearance of skin lesions); SD = stable disease (<25% increase to <50% clearance of skin lesions); PD = progressive disease (≥25% increase in disease)

Conclusion: Combination topical IMQ and low-dose RT was well-tolerated and may produce a systemic anti-tumor response in some patients, as demonstrated by clinical and histological improvements in treated and untreated lesions.

Learning Objectives:

1. Participants should be able to describe the rationale for using combination low-dose targeted radiotherapy (RT) and topical imiquimod (IMQ) in the treatment of mycosis fungoides (MF).
2. Participants should be able to describe the clinical responses seen in treated and untreated lesions after RT/IMQ treatment.

P47 New Onset and Rapid Progression of Cutaneous T-Cell Lymphomas in Association with Immune Checkpoint Inhibitor Therapy: a Systematic Review

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Introduction: Immune checkpoint inhibitors (ICIs) have been associated with paradoxical phenomena such as tumor pseudoprogression and hyperprogressive disease. This systematic literature review summarizes available reports of cutaneous T-cell lymphomas (CTCL) developing (*de novo*) or accelerating (pre-existing) during ICI therapy.

Methods, Results: A systematic search of PubMed, Embase, and Web of Science was conducted according to PRISMA guidelines. Eligible publications included clinical trials, case series, and case reports. Extracted data included patient characteristics, CTCL subtype, ICI regimen, timing, clinical presentation, histopathology, outcomes, and proposed mechanisms.

Across 11 eligible studies, 11 patients were identified. Seven patients developed new onset CTCL, while four experienced rapid progression of pre-existing disease during treatment with immunotherapy. Most ICIs were prescribed for the treatment of metastatic melanoma or renal cell carcinoma. One clinical trial enrolled patients with CTCL. The interval between ICI initiation and CTCL onset/acceleration ranged from 12 days to 18 months. Clinical presentations included erythroderma, panniculitis-like nodules, and indurated plaques. Outcomes varied: some patients deteriorated rapidly and died within months, whereas others achieved remission following ICI discontinuation and additional treatment.

Conclusion: These reports highlight a rare but clinically relevant possible association between ICI therapy and new onset or rapid progression of pre-existing CTCL. Clinicians should maintain vigilance for atypical cutaneous eruptions or sudden disease acceleration in patients receiving ICIs. This issue is particularly important as ICI monotherapy and combination regimens are actively being explored in clinical trials as novel therapies for CTCL. Larger studies are required to clarify risk factors, clinical management, and underlying mechanisms.

Learning Objectives:

1. Summarize published reports of de novo or rapidly progressive cutaneous T-cell lymphoma occurring during immune checkpoint inhibitor therapy.
2. Identify the timing and clinical presentations reported in these cases.
1. Discuss implications for clinical monitoring and management as immune checkpoint inhibitors are explored as therapies for cutaneous T-cell lymphoma.

LATEBREAKING ABSTRACTS

P48 Disproportionate Representation of Intellectual Disability and Higher Fitzpatrick Skin Types Among Patients Presenting with Tumor-Stage Cutaneous T-Cell Lymphoma

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Introduction: Cutaneous T-cell lymphoma (CTCL), most commonly mycosis fungoides (MF), is typically diagnosed at early stages, and tumor-stage presentation at diagnosis is fairly uncommon. Delayed diagnosis may reflect underlying clinical and systemic disparities. We aimed to characterize patients presenting with tumor-stage CTCL at diagnosis and identify patterns associated with delayed diagnosis.

Methods, Results: We performed a retrospective review of 239 patients with MF at a single academic center. Lesion type at diagnosis and maximum lesion stage over the disease course were recorded. Patients presenting with tumor-stage disease (stage IIB+) were identified, and clinical characteristics including intellectual disability (ID), Fitzpatrick skin type (FST), time to diagnosis, and prior diagnoses were analyzed.

At diagnosis, 80.0% (n = 193) of patients presented with patch-stage disease, 17.6% (n = 41) with plaque-stage, and 2.1% (n = 5) with tumor-stage disease. Over the disease course, an additional 10 patients progressed to tumor-stage disease following initial diagnosis. Among those presenting with tumor-stage disease, all patients with documented ID in the cohort were represented in this group (3/5, 60%). Time from symptom onset to diagnosis ranged from 6 months to 10 years, with most patients (4/5) experiencing prolonged delays of ≥ 5 years. All patients had prior diagnoses of inflammatory dermatoses, most commonly psoriasis or eczema, prior to CTCL diagnosis. The majority (4/5) had higher FST (IV–VI); the only patient with lighter skin type (I) had the shortest time to diagnosis (6 months).

Conclusion: Tumor-stage CTCL at diagnosis is rare and may represent diagnostic delay. The overrepresentation of patients with ID and higher FST, combined with extended time to diagnosis and frequent misdiagnosis, highlights potential disparities in early recognition. These findings support increased clinical vigilance in vulnerable populations such as patients with ID and higher FST.

Learning Objectives:

1. Recognize clinical and demographic factors associated with tumor-stage presentation of cutaneous T-cell lymphoma, including intellectual disability and Fitzpatrick skin type.
2. Identify patterns of diagnostic delay in CTCL, including prolonged time to diagnosis and common misdiagnoses such as eczema and psoriasis.
3. Discuss reasons for heightened clinical suspicion in patients with persistent or atypical dermatoses, particularly in vulnerable populations at risk for delayed diagnosis.

P49 Deruxtecan-Based Antibody-Drug Conjugate Targeting TCR-Vβ2 for the Treatment of Cutaneous T Cell Lymphoma

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Introduction: A challenge in the development of effective and safe immunotherapies for T cell lymphomas and leukemias is the lack of a unique marker on malignant vs healthy T cells. We observed that malignant T cells from advanced cutaneous T cell lymphoma (CTCL) patients express a clone-defining T cell receptor (TCR), with Vβ2 being the most common represented variable region of the >20 Vβ families. Since each Vβ gene is expressed by only a small fraction (~3–9%) of the overall T cell population, a patient-matched Vβ-specific immunotherapy may be a safer strategy for eliminating CTCL cells. We previously generated anti-Vβ2 chimeric antigen receptor (CAR)-T cells using purified T cells from healthy donors as a potential patient-matched Vβ-specific immunotherapy. However, to overcome the production cost and logistical challenges of generating CAR-T immunotherapies, we have now developed antibody-drug conjugate (ADC) prototypes using different conjugation strategies and payloads.

Methods, Results: First, we show that the antibody binds to Vβ2 regardless of the paired Vα chain. Then, using a Lysolight internalization assay, we show that a Fc-inactivated humanized anti-Vβ2 antibody is readily internalized in patient and Jurkat target cells. Deruxtecan (Dxd), a topoisomerase 1 inhibitor, was then conjugated to the anti-Vβ2 antibody via thiol-maleimide chemistry (drug-antibody ratio of 8). We show that this anti-Vβ2-Dxd ADC can effectively and specifically kill Vβ2 Jurkat cells in vitro. Finally, to assess the anti-Vβ2-Dxd ADC in vivo, complimentary mouse xenograft models using NSG mice were generated by intravenous or subcutaneous injection of luciferase-expressing Vβ2+ Jurkat cells to model leukemia and lymphoma, respectively. In vivo preclinical imaging revealed that tumor growth was substantially suppressed in mice treated with anti-Vβ2-Dxd ADC (4 mg/kg i.p.) when compared to control-treated mice.

Conclusion: Overall, we demonstrate a strategy of targeting the TCRVβ chain with ADCs for the treatment of Vβ+ clonal CTCL and other T-cell-driven malignancies.

Learning Objectives:

The TCR can be targeted as a potential strategy for the treatment of T-cell-driven malignancies.

P50 Primary Cutaneous Innate Lymphoid Lymphoma

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Introduction: Innate lymphoid cells (ILCs) mediate innate immunity at barrier sites like the skin but lack T-cell receptor gene rearrangements and diagnostic pan-T or pan-B markers. We report an extraordinary case of mycosis-fungoides like primary cutaneous lymphoma characterized by an innate lymphoid phenotype, highlighting a unique diagnostic challenge with potential implications for therapy.

Case Report: A 73-year-old man with a 14-year history of presumed, refractory mycosis fungoides (MF) presented with extensive patches and plaques. Repeated biopsies demonstrated epidermotropism of an atypical monomorphic lymphocytic population; however, the cells consistently lacked T-cell receptor (TCR) clonality and lymphocyte markers (CD3, CD4, CD8, CD20, CD30, CCR4). To resolve the clinicopathologic discrepancy and reassess therapeutic strategization, comprehensive profiling was performed. Tissue flow cytometry revealed an unusual CD45+, CD25+, and cytoplasmic TIA-1+ phenotype devoid of markers including CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD14, CD19, CD20, CD22, CD26, CD34, CD38, CD42b, CD56, CD61, CD117, CD279, TCR-gd, cytoplasmic MPO, cytoplasmic CD3, or cytoplasmic CD79a. Genomic sequencing identified a clonal in-frame LMNA::ALK fusion, confirmed by ALK nuclear staining, alongside pathogenic *DNMT3A* and *TP53* mutations. Four additional prior specimens demonstrated positive nuclear ALK staining of the atypical lymphocytic population. GATA3 labels a subset of the atypical population and TBET was negative; mRNA expression data demonstrated increased *GATA3* mRNA and negative expression for *TBX2*. Imaging showed no systemic disease. These findings suggest a diagnosis of primary cutaneous innate lymphoid lymphoma, bearing an immunophenotype and absence of TCR gene rearrangements that resemble skin-resident ILC2 cells. This case demonstrates that cutaneous lymphomas can arise from ILC lineages, clinically mimicking MF while necessitating dedicated genomic studies and special stains for accurate detection and disease confirmation. Recognizing this novel entity is critical, as properties of its cell of origin, such as IL-13 production and sensitivity to retinoid receptor agonists, may unveil novel, targeted therapeutic pathways.

Learning Objectives:

- Innate lymphoid cells mediate innate immunity at barrier sites and typically express CD45 and are negative for B, T, and myeloid lineage markers and lack TCR rearrangements.
- A recurrent expression of a fusion can be used to demonstrate monoclonality in cases lacking T-cell receptor clonality.
- In cases of clinical and histologic suspicion for cutaneous lymphoma, additional molecular and genomic studies should be performed if standard immunohistochemistry and T-cell clonality do not result in a diagnosis.

P51 Epidermotropic, Cytotoxic, Alk+ T-Cell Lymphoma: Appraisal of a Discrete Pattern of Disease

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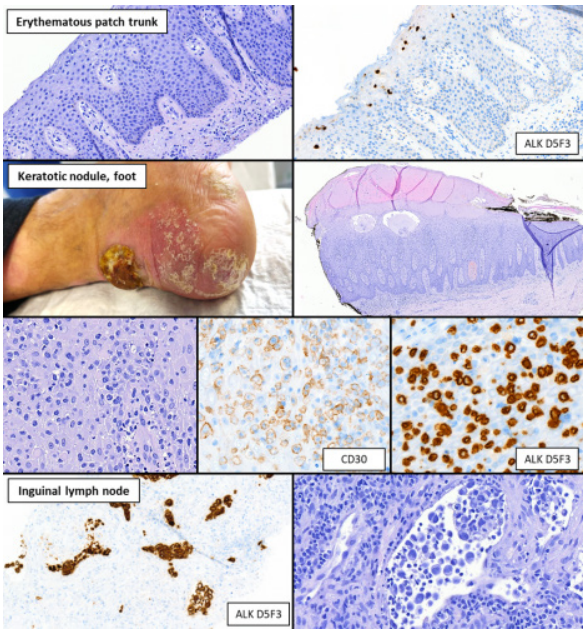
Introduction: ALK-positive T-cell lymphoma (TCL) is to be considered a nodal/systemic disease, until proven contrary.

Rare patients demonstrate a mycosis fungoides (MF)-like clinical and histological pattern [PMID 38780617], challenging the conventional knowledge and posing major clinical-pathologic difficulties, which we aim at discussing with the following, novel case.

Case Report: A 57-year-old male under follow-up for psoriasis was diagnosed in August 2024 with ALK-positive anaplastic large cell lymphoma (ALK+ ALCL), following biopsy of a keratotic nodule on the left foot. Serial PET imaging showed initial disease limited to the left foot and regional lymph nodes, with subsequent near-complete metabolic regression under a watchful waiting approach. By January 2026, clinical worsening of "psoriasis" and persistent nodal involvement prompted new biopsies of skin and inguinal lymph node at our Institution.

Skin biopsies (figure 1) revealed psoriasiform hyperplasia, with pronounced spongiosis and keratosis on the foot, also featuring Civatte-type bodies and a uniquely epidermotropic infiltrate of large, pleomorphic cells with a CD4+/perforin+/CD30+^{dim}/ALK1+^{dim}/ALK-D5F3+^{high} phenotype; lymph node biopsy proved exclusive intralymphatic involvement. NGS demonstrated an unusual *RANBP2::ALK* rearrangement. PET staging revealed a disease limited to the skin and left inguinal/iliac lymph nodes, without distant nodal nor visceral involvement, and negative bone marrow biopsy.

Differential diagnosis includes nodal ALK+ ALCL with cutaneous involvement versus a MF–like, epidermotropic, ALK+ TCL (stage IIB-type disease, EORTC criteria).



Discussion: Besides the very limited experience, existent data [PMID 38780617] suggest the presence of a recurrent pattern of disease, namely of (CD4-positive), primary cutaneous epidermotropic, cytotoxic, ALK+ TCL. A major challenge in dealing with this subset includes its prodromal phases, easily misinterpreted as inflammatory dermatosis.

Data on its optimal management is far from being conclusive: a MF-like approach is currently chosen, but depending on CD30 and, most notably, ALK expression, a targeted therapy could be envisaged in advanced stages.

Learning Objectives:

1. To discuss the clinicpathologic picture of primary cutaneous T-cell lymphomas featuring ALK expression.
2. To discuss the challenges and the grey zones in the current lymphoma classifications

P52 Adult T-Cell Leukemia/Lymphoma Emerging During Dupilumab Therapy for Severe Atopic Dermatitis: Should We Screen for HTLV-1?

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Introduction: The clinical distinction between atopic dermatitis (AD) and cutaneous T-cell lymphomas is challenging, particularly in patients with primary immunodeficiencies such as Wiskott-Aldrich Syndrome (WAS). Dupilumab has revolutionized AD treatment; however, increasing reports suggest it may unmask or reveal underlying T-cell lymphoproliferative disorders. This case reports the emergence of Adult T-cell Leukemia/Lymphoma (ATLL) in a patient with WAS during treatment with Dupilumab

Case Report: A 49-year-old man with WAS (characterized by immunodeficiency, chronic thrombocytopenia and severe AD) initiated Dupilumab in 2024. Despite initial cutaneous improvement, he developed new pruritic plaques involving approximately 40% of body surface area after one year, leading to treatment discontinuation under suspicion of a drug-related eruption. Skin biopsy demonstrated a folliculotropic atypical T-cell infiltrate (CD3+, CD4+, partial CD7 loss), suggestive of mycosis fungoides. Peripheral blood and bone marrow flow cytometry identified an abnormal CD4+ T-cell population with loss of CD7. HTLV-1 serology was positive and confirmed by reference testing. PET/CT revealed metabolically active lymphadenopathy. The patient was diagnosed with chronic-type Adult T-cell Leukemia/Lymphoma (ATLL), and is currently managed with skin-directed therapy with plans for pegylated interferon.

Discussion: This case highlights the diagnostic challenge of differentiating inflammatory dermatoses from early T-cell lymphoproliferative disorders. Clinical progression with new lesions following biologic therapy prompted further investigation. Dupilumab may alter immune signaling and unmask underlying malignancy; in this context, the patient's underlying Wiskott–Aldrich syndrome may have contributed to a permissive environment for clonal expansion. This case raises the critical question of whether HTLV-1 screening should be considered prior to initiating dupilumab in patients with refractory dermatitis, particularly in endemic regions or in those with complex immune histories.

Learning Objectives:

1. Evaluate the diagnostic challenges of identifying cutaneous lymphomas in patients with primary immunodeficiencies and chronic eczematous backgrounds.
2. Recognize the potential risk of Adult T-cell Leukemia/Lymphoma (ATLL) unmasking or progression following the initiation of Dupilumab.
3. Evaluate the role of HTLV-1 screening prior to biological therapy in patients with atypical or refractory dermatitis.

P53 Adult T-Cell Leukemia/Lymphoma Mimicking Indolent Cutaneous Lymphoma: The Role of HTLV-1 and Re-biopsy in Endemic Regions

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Introduction: Adult T-cell Leukemia/Lymphoma (ATLL) is a mature T-cell malignancy associated with HTLV-1. Cutaneous manifestations are common and highly polymorphic, frequently mimicking other cutaneous lymphoproliferative disorders such as mycosis fungoides (MF) or lymphomatoid papulosis (LyP), creating significant diagnostic challenges. Chile is considered an HTLV-1 endemic region, with a moderate prevalence of approximately 0.1%, lower than that observed in highly endemic areas.

Case Report: A 69-year-old woman with HTLV-1 associated spastic paraparesis presented with several months of pruritic papules and plaques. Initial histopathology suggested LyP, however, the patient was refractory to clobetasol, methotrexate and phototherapy (UVB/PUVA).

A second biopsy demonstrated a diagnostic challenge, as samples showed CD3+, CD4+, CD8+, CD25+, CD2+, CD5+, CD40+, CD7+ infiltrate with a Ki67 of 70%, consistent with ATLL, mycosis fungoides or peripheral T-cell lymphoma with cutaneous involvement. Finally, a third biopsy confirmed CD4+, CD7-, CD25+ ATLL. Initially classified as smoldering ATLL (4.7% abnormal T cells in peripheral blood flow cytometry, sCD25 4839 U/mL), the patient rapidly progressed to acute disease with severe paraneoplastic hypercalcemia (>20.1 mg/dL), CD30 expression, and a marked increase in sCD25 levels (7130 U/mL). Treatment was escalated to CHOEP chemotherapy followed by PEG-IFN and zidovudine.

Discussion: This case underscores that in HTLV-1 endemic regions or known carriers, any indolent lymphoproliferative diagnosis must be continuously reevaluated if clinical progression or therapeutic failure occurs, and HTLV-1 testing should be mandatory for all cutaneous T-cell malignancies in endemic regions. The transition from smoldering to acute progression can be sudden, so monitoring sCD25 and CD30 could serve as essential harbingers of imminent aggressive transformation

Learning Objectives:

1. Identify Adult T-cell Leukemia/Lymphoma (ATLL) as a clinical mimic of indolent cutaneous lymphoproliferative disorders like mycosis fungoides or lymphomatoid papulosis.
2. Highlight the importance for mandatory HTLV-1 testing in all patients with cutaneous T-cell lymphomas in endemic regions.
3. Identify paraneoplastic syndromes and elevated sCD25/CD30 as markers of acute transformation from smoldering ATLL.

P54 Imaging Beyond Staging in Primary Cutaneous Marginal Zone Lymphoma: Interim Analysis of a Multi-Institutional Retrospective Study

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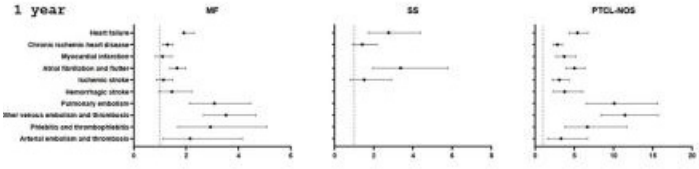
Introduction: Primary cutaneous marginal zone lymphoma (PCMZL) is a rare, indolent B-cell lymphoma associated with excellent prognosis. Recent reclassification as a lymphoproliferative disorder by the International Consensus Classification has introduced uncertainty regarding recommended staging workup. In this ongoing multi-institutional retrospective cohort study, we aimed to evaluate the role of imaging during staging in identifying clinically significant comorbidities in patients with PCMZL.

Methods, Results: Demographics, medical history, staging, and disease course of PCMZL patients seen at Columbia University, New York University, Johns Hopkins University, University of Pennsylvania, and Pennsylvania State University between 2010-2025 were analyzed. We excluded patients with concurrent hematological malignancy or incomplete records.

One-hundred-fifty-eight patients with PCMZL were included. Patient demographics were consistent with prior literature, with mean age 59.1 years and male predominance (59%). Associated comorbidities were documented in 107 patients (68%), including inflammatory gastrointestinal disorders (36%), infectious disorders (24%), cutaneous malignancies (21%), non-cutaneous malignancies (21%), and autoimmune disorders (20%). Staging positron emission tomography-computed tomography (PET-CT) was performed in 113 patients (72%). Abnormalities detected on imaging included lymphadenopathy (n=21, 13%) and other suspicious findings (n=66, 42%), for example gastric thickening or pulmonary nodules. Four non-PCMZL neoplasms were identified by imaging for PCMZL workup, including breast cancer, lung cancer, renal cell carcinoma, and meningioma. Detection of gastric uptake in two patients by staging PET-CT led to diagnosis of gastritis. Notably, in one patient, PCMZL lesions resolved after treatment of inflammatory bowel disease.



Conclusion: Our findings highlight a possible association between PCMZL diagnosis and states of chronic antigen stimulation, with utility of imaging in uncovering occult comorbidities in PCMZL patients. Prospective studies are needed to validate these associations to better understand pathogenesis and appropriate workup, particularly regarding the role of PET-CT.

Learning Objectives:

1. Identify comorbid conditions associated with PCMZL, including inflammatory, infectious, autoimmune, and malignant processes.
2. Apply the understanding of a possible relationship between chronic antigen stimulation and PCMZL pathogenesis to inform diagnostic workup considerations (e.g. imaging).
3. Discuss the role of staging imaging in patients with PCMZL following recent disease reclassification.

P55 Cutaneous and Peripheral T-Cell Lymphomas Increase the Risk of Cardiovascular and Thromboembolic Events: a Retrospective TriNetX Cohort Study

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Introduction: Background: Systemic inflammation in cutaneous T-cell lymphoma (CTCL) may increase the risk of cardiovascular (CV) and thromboembolic (TE) events.

Objective: Assessing CV and TE risk in CTCL, including mycosis fungoides (MF) and61 Sézary syndrome (SS) compared with peripheral T-cell lymphoma, not otherwisespecified (PTCL-NOS).

Methods, Results: Methods: In this retrospective cohort study using the TriNetX database, patients with MF, SS, and PTCL-NOS were compared to propensity score–matched healthy controls for CV (heart failure, atrial fibrillation (AF)/flutter, ischemic heart disease, myocardial infarction, stroke) and TE outcomes (pulmonary embolism, other venous thromboembolism, and arterial embolism) at different time points.

Results: A gradient of increasing risk was observed from MF (1-year risk ratio (RR) = 1.6–3.5) to SS (1-year RR = 2.8–5.2) to PTCL-NOS (1-year RR = 5.0–11.5) for AF/flutter, heart failure, and venous TE (VTE). Pulmonary embolism showed the strongest associations. Arterial outcomes were weak or inconsistent in MF and SS but markedly elevated in PTCL-NOS.

Conclusion: Conclusions: CTCL are associated with increased risk of heart failure, AF, and VTE, which seems to be independent of traditional CV risk factors, with substantially higher risks in SS and PTCL-NOS.

Learning Objectives:

Thromboembolic events should be carefully assessed and asked for in CTCL and PTCL.

P56 IL4Rα Blockade Inhibits Proliferation of Malignant Lymphocytes and the Immunosuppressive Tumor Microenvironment of Mycosis Fungoides

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Introduction: Limited therapeutical options are available for patients with advanced-stage mycosis fungoides (MF), and the 5-year survival rate is 25%. Due to its critical role in MF pathogenesis, the IL4/IL13 pathway presents a promising target for treatment. Here we analyzed blocking of IL4Rα, the common subunit of the IL4 and IL13 receptors, within the advanced-stage MF cutaneous tumor microenvironment (TME).

Methods, Results: Cellular Indexing of Transcriptomes and Epitopes by sequencing was employed to assess the transcriptional profile of the cells expressing the IL4 and IL13 receptors within the advanced MF TME. We combined IL4Rα inhibition by dupilumab in *ex vivo* skin explants from advanced MF patients with single-cell transcriptome and machine learning analysis to identify the molecular mechanisms of IL4Rα signaling within the MF skin lesions. Multicolor immunofluorescence microscopy was employed to validate molecular findings.

REGN668 inhibits patient-specific processes in malignant lymphocytes; however, we also identified downregulation of common pathways among patient samples including those associated with cell cycle progression, PI3K/AKT signaling, JAK/STAT signaling, DNA damage/repair, and TP53 regulation. Furthermore, we showed that IL4Rα blockade in the TME of advanced MF downregulates multiple immunosuppressive pathways associated with myeloid-derived suppressor cell and $LAMP3^+$ dendritic cell recruitment and function, cytokine production and antigen presentation in B cells as well as differentiation and degranulation of mast cells.

Conclusion: These results provide new insights into advanced MF tumorigenesis and show that the effects of IL4Rαblockade are specific to the STAT6 pathway, inhibiting proliferation of malignant lymphocytes as well as repressing several immunosuppressive mechanisms within the MF TME. However, the extensive genetic, transcriptional, and functional heterogeneity across MF patients indicates that inhibition of multiple driver pathways and a personalized therapeutic approach will be important for developing new therapeutic strategies against this disease.

Learning Objectives:

- IL4/IL13 inhibition by targeting IL4Rα reduces malignant lymphocyte proliferation in advanced MF skin tumors
- IL4Rα blockade reverts multiple immunosuppressive mechanisms by inflammatory cells in the advanced MF tumor microenvironment.