STANFORD MULTIDISCIPLINARY CUTANEOUS LYMPHOMA PROGRAM (MCLP)

The Stanford Multidisciplinary Cutaneous Lymphoma team offers expert treatment for patients with cutaneous lymphomas, including mycosis fungoides, Sézary syndrome, CD30+ lymphoproliferative disorders (lymphomatoid papulosis and anaplastic large cell lymphoma), subcutaneous panniculitis-like T-cell lymphoma, gamma-delta T-cell lymphoma, CD8+ aggressive epidermotropic T-cell lymphoma, NK/T-cell lymphoma, other unspecified cutaneous peripheral T-cell lymphomas, and cutaneous B-cell lymphomas. Our physicians subspecialize in treating these types of cancers, and have extensive expertise in handling the most complicated cases. In fact, we serve as the consultants to the experts. Care among specialists is tightly integrated.

Innovative Discoveries and Treatments
The Stanford team continues its leadership in bringing the state-of-the-art technology platforms to the clinics testing new diagnostic and prognosticating tools and establishing biomarkers of clinical outcome. Our multidisciplinary approach allows the most comprehensive and personalized management of each patient. Moreover, we offer the newest or novel cancer treatments, such as new targeted and immunotherapies, including ones that are only available at Stanford. Examples of the new therapies available at Stanford and their clinical development updates:

- Targeted therapies that attack tumor surface proteins, aberrant epigenetic regulation, signaling or cell survival pathways, or the microenvironment.
- Mogamulizumab (KW-0761) is a bioengineered, humanized monoclonal antibody against CCR4, selectively expressed on tumor cells; the defucosylated technology provides enhanced efficacy. Stanford’s leadership has led to the successful completion of the phase 3 trial, the results of which is expected to lead to FDA approval.
- Brentuximab vedotin (SGN-35) is an antibody-drug-conjugate that targets CD30, commonly expressed on tumor cells in cutaneous T-cell lymphomas. Stanford led clinical trial in cutaneous T cell lymphoma have shown impressive activity allowing brentuximab vedotin to be listed in standard of care guidelines. Stanford’s trial served as the basis for the phase 3 clinical trial that will lead to official FDA approval.
• Immune checkpoint blockade such as anti-PD-1 monoclonal antibody that unleashes the antitumor effector T cells that fight off malignant T cells in mycosis fungoides and Sézary syndrome. Promising clinical activity has been observed with pembrolizumab and additional immune combination therapy trial is planned.

• Novel macrophage checkpoint blockade, anti-CD47 monoclonal antibody, specifically discovered at Stanford, followed by continued clinical development in solid tumors and lymphoma including cutaneous T cell lymphoma. Blocking the checkpoint with the antibody allows effective phagocytosis of the malignant cells by patient’s own macrophages.

• Anti-KIR3DL2 monoclonal antibody therapy in cutaneous T cell lymphoma. KIR3DL2 is a highly expressed molecule on neoplastic T cell in CTCL, including transformed mycosis fungoides and Sézary syndrome. This antibody works by stimulating the patient’s own immune system to attack the KIR3DL2 expressing cancer cells.

• The oligonucleotide inhibitor (anti-miR) of miR-155-5p in patients with mycosis fungoides. MicroRNAs (miRNAs) are small, non-coding RNAs that act as negative regulators of gene expression. miR-155-5p has been implicated in tumor progression in mycosis fungoides, thus this anti-miR therapy may result in antitumor effects.

• Improved version of denileukin diftitox, a recombinant fusion protein that targets IL-2 receptor (CD25) commonly present on tumor cells in cutaneous T-cell lymphoma. Moreover, CD25 is expressed on a negative immune regulator, namely the regulatory T cells, thus treatment with this agent also depletes these negative regulator cells, whereby enhancing the antitumor immune activity. Thus, this agent has both direct action against the tumor cells as well as a bonus indirect effect by augmenting the host immune activity against the tumor cells.

• Low-dose (12 Gy) total skin electron beam therapy combined with recombinant human IL-12, a potent and broad immune activator, to improve the duration of clinical benefit of the total skin radiation therapy. IL-12 is a potent immune enhancing cytokine that works to synergistically boost anti-tumor immune response when combined with radiation therapy.

• Novel/newer topical agents including topical histone deacetylase inhibitor. Preliminary results show encouraging clinical activity with great tolerability, thus confirming that the topical application of histone deacetylase inhibitors can potentially clear patients skin disease without the side effects of the systemically administered counterpart.

• Non-myeloablative allogeneic hematopoietic stem cell transplantation (HSCT) using total skin electron beam therapy, total lymphoid irradiation (TLI), and anti-thymocyte globulin (ATG) as novel preparatory regimen for patients with mycosis fungoides and Sézary syndrome. Stanford’s “protective” conditioning regimen allows patients to have curative results with much improved safety profile than conventional allogeneic stem cell transplantation regimens.

• Newer molecular diagnostic methods including TCR high throughput sequencing that offers superior sensitivity and specificity over conventional tools for the identification and monitoring of clonal malignant T cells. This type of technology is actively used to follow cancer activity that is not measurable by conventional methods, thus better defining and predicting if patients can be in long-term remission. Stanford has led the first application of this high throughput technology in patients who received stem cell transplantation and demonstrated that the patients who are clear of molecular disease using this method are more likely to have longer lasting disease-free states and may be cured. The same method is also used to identify distinct malignant clones thus differentiating lymphoma from benign or inflammatory mimics, leading to early and/or more definitive diagnosis.

• Sophisticated in-depth next generation sequencing of tumor tissue and blood to identify driver/actionable new targets, bolstering our investigations towards delivering personalized/precision medicine. Stanford has led investigations to help identify key pathways and molecules used by tumor cells for their survival and spread of cancer. We have developed clinical trials that use therapies that are available or engineered to target these aberrant molecules or pathways.

**Unique Integrated Multidisciplinary Care**

The Stanford Multidisciplinary Cutaneous Lymphoma Clinic (MCLC) is a national leader in the diagnosis and treatment of patients with cutaneous lymphomas. In operation for over 35 years at Stanford, the MCLC (similar to a tumor board) is held twice weekly and patients are jointly evaluated and managed by cutaneous, medical, and radiation oncologists, stem cell transplantation experts, and pathologists who each have expertise in cutaneous lymphoma. Stanford is unique in offering this interdisciplinary care in cutaneous lymphoma to provide the most comprehensive and optimal care for patients with this very rare group of lymphomas. Our Interdisciplinary collaboration extends beyond our clinical care and integrates into our research activities thus bringing new discoveries that translate into advancing our clinical practice across all related disciplines.
International Leadership

The Stanford MCL team led the efforts in establishing the Cutaneous Lymphoma International Consortium (CLIC), an international collaborative network of CL expert centers for large scale studies. There are more than 60 international centers that have joined the CLIC goals to participate in impactful clinical and translational research. Stanford currently serves as CLIC's coordinating data center for the collection and management of clinical, pathology, and molecular data linked with a federated (“virtual”) Biobank establishment at each participating center. This CLIC Biobank will serve as an invaluable repository of clinical (patient) samples linked with prospectively collected clinical and pathology annotation for future translational research. Through this mechanism, key scientific discoveries reported from an expert center can be efficiently validated in a larger study at an international level. Thus our international leadership and large scale collaboration effectively brings the world experts together for greater impact.

CUTANEOUS LYMPHOMA CLINICAL TRIALS

To learn more about active Lymphoma clinical trials, please visit cancer.stanford.edu/trials or cutaneoulyphoma.stanford.edu

- Prospective Multicenter International Observational Study for Determination of a Cutaneous Lymphoma International Prognostic Index Model and Impact of Major Therapies in Patients with Advanced Mycosis Fungoides and Sézary Syndrome
- Open-Label, Multi-Center, Randomized Study of Anti-CCR4 Monoclonal Antibody KW-0761 (Mogamulizumab) Versus Vorinostat in Subjects with Previously Treated Cutaneous T Cell Lymphoma
- A Randomized, Open-Label, Phase 3 Trial of Brentuximab Vedotin Versus Physician’s Choice (Methotrexate or Bexarotene) in Patients with CD30-positive Cutaneous T Cell Lymphoma
- Open Label, Multicenter Phase I Study of IPH4102, a Humanized Anti-KIR3DL2 Monoclonal Antibody, in Patients with Relapsed/Refractory Cutaneous T-cell Lymphomas
- A Phase 2 Investigator-Initiated Study of MK-3475 (Anti-PD-1, Pembrolizumab) for the Treatment of Relapsed/Refractory Mycosis Fungoides/Sézary Syndrome
- A Single Arm, Open-Label Study to Evaluate the Safety, Tolerability and Preliminary Efficacy of NM-IL-12 (rHuIL-12) in Patients with Cutaneous T Cell Lymphoma (CTCL) Undergoing Low Dose Total Skin Electron Beam Therapy (TSEBT)
- A Phase 1 Dose-Ranging Study to Investigate the Safety, Tolerability, and Pharmacokinetics of MRG-106 (anti-miR-155-5p) Following Local Intratumoral and Subcutaneous Injection in Patients with Cutaneous T Cell Lymphoma (CTCL), Mycosis Fungoides (MF) Sub-type
- Phase III Study to Demonstrate Safety and Efficacy of E7777 (Denileukin Diftitox) in Persistent or Recurrent Cutaneous T Cell Lymphoma
- A Phase III Multicenter Randomized, Double-Blind, Placebo-Controlled Study to Determine the Efficacy of Topical SGX301 (Synthetic Hypericin) and Fluorescent-Bulb Light Irradiation for the Treatment of Cutaneous T Cell Lymphoma
- A Phase II Study of Non-myeloablative Allogeneic Transplantation Using Total Lymphoid Irradiation (TLI) and Antithymocyte Globulin (ATG) In Patients with Cutaneous T Cell Lymphoma
- A First-In-Human Phase 1 Dose Escalation Trial of Hu5F9-G4 In Patients With Advanced Solid Malignancies: Cutaneous T Cell Lymphoma (CTCL) Translational Cohort
- A Phase 1 Trial of Duvelisib (IPI-145) in Combination with Either Romidepsin or Bortezomib in Relapsed/Refractory T cell Lymphomas.
SELECTED PUBLICATIONS BY STANFORD MCLP


