



STANFORD CUTANEOUS LYMPHOMA PROGRAM

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The Stanford multidisciplinary cutaneous lymphoma team offers expert treatment for patients with cutaneous lymphomas, including mycosis fungoides, Sezary 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**. Care among specialists is tightly integrated.

STANFORD MULTIDISCIPLINARY CUTANEOUS LYMPHOMA PROGRAM (MCLP)

Innovative Treatments and Technologies. The Stanford team is commonly involved in testing new diagnostic tools, biomarkers, or cancer treatments. Examples include:

- Targeted therapies that attack tumor surface proteins, aberrant epigenetic regulation, signaling or cell survival pathways, or microenvironment
- Mogamulizumab (KW-0761) is a bioengineered, humanized monoclonal antibody against CCR4, selectively expressed on tumor cells; the defucosylated technology provides efficacy
- Brentuximab vedotin (SGN-35) is an antibody-drug-conjugate that targets CD30, commonly expressed on tumor cells in cutaneous T-cell lymphomas
- 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
- Low-dose (12 Gy) total skin electron beam therapy combined with vorinostat, a potentially radiation enhancing agent, to reduce overall toxicity of radiation while improving efficacy
- Novel/newer topical agents including topical histone deacetylase inhibitor
- New immunotherapy strategies that co-stimulate immune cells or block immune checkpoints
- 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 Sezary syndrome
- Newer techniques utilizing rapid molecular diagnostic methods or new immunostains for earlier and more accurate diagnosis
- Sophisticated sequencing of tumor tissue and blood to identify driver/actionable new targets, bolstering our investigations towards delivering personalized medicine

Multidisciplinary Care. The Stanford Multidisciplinary Cutaneous Lymphoma Clinic (MCLC) is a national leader in clinical/translational research and treatment of patients with cutaneous lymphomas. In operation for over 30 years at Stanford, the MCLC (similar to a tumor board) is held twice weekly and patients are co-evaluated and co-managed by cutaneous, medical, and radiation oncologists, 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.

STANFORD CUTANEOUS LYMPHOMA PROGRAM

STANFORD MCLP RESEARCH BREAKTHROUGHS

- **Novel *in situ* vaccination strategy** combining intratumoral CpG, a powerful immune-stimulatory agent, and local radiation, to circumvent the need to produce labor-intensive and time-consuming *ex vivo* vaccine product. This *in situ* strategy effectively provided tumor antigens from dying tumor cells (induced by local RT) to antigen presenting cells (APCs) and activated these APC to present their engulfed antigens to T-cells. This immune-stimulatory strategy is now being applied to augment anti-tumor responses in patients who have disease progression after allogeneic HSCT.
- Demonstration of how **traditional therapies are used more effectively** with improved clinical benefit to the patient with dramatic efficacy while lessening side effects. This has been exemplified by the modification of our total skin electron beam therapy (TSEBT), known as the “Stanford TSEBT technique,” by reducing the total dose by two-thirds this **novel low-dose total skin electron beam therapy** results in dramatic clearing of disease with significantly less toxicity. The lower dose approach allows patients to receive total skin therapy multiple times in their course. Strategies to enhance clinical activity by combining with other therapies are being actively explored.
- Establishment and strengthening of collaborative network with leading genomics groups at Stanford to **decipher the molecular mechanism of cutaneous lymphoma and discover new driver/actionable targets** for development of newer therapies. Our initial investigation of whole transcriptome sequencing using RNA-Seq in Sezary syndrome has already identified novel Sezary cell-associated transcripts.
- Curative or long-term clinical benefit is demonstrated with **novel allogeneic HSCT regimen** utilizing preparatory regimen of total skin electron beam therapy (TSEBT), total lymphoid irradiation (TLI) and antihymocyte (ATG). Stanford investigators have shown that TLI/ATG conditioning results in effective graft versus lymphoma effect with reduced complication of graft versus host disease. The TSEBT contributes towards more effective elimination of tumor cells in the skin, a site where complete response has been difficult to attain with systemic therapies. Furthermore, we are exploring the **utility of deep sequencing of patient-specific T-cell receptor to monitor minimal residual disease**, thus allowing the most sensitive and specific approach to determine clinical outcome.

CUTANEOUS LYMPHOMA CLINICAL TRIALS

To learn more about active lymphoma clinical trials: cancer.stanford.edu/trials or cutaneouslymphoma.stanford.edu

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 [LYMNHL0099]

Phase 1B Study to Assess the Safety, Pharmacodynamics and Pharmacokinetics of SHP-141, Administered Topically to Patients with Stage IA, IB or IIA Cutaneous T-Cell Lymphoma [LYMNHL0090]

Exploratory Pilot Study of Brentuximab Vedotin (SGN-35) in Patients with Mycosis Fungoides and Sezary Syndrome with Variable CD30 Expression Level [LYMNHL0089]

A Randomized, Open-Label, Phase 111 Trial of Brentuximab Vedotin (SGN 35) Versus Physician’s choice (Methotrexate or Bexarotene) in Patients with CD30-Positive Cutaneous T-Cell Lymphoma [LYMNHL0095]

Analysis of Cutaneous and Hematologic Disorders by High-Throughput Nucleic Acid Sequencing [LYMNHL0091]

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 [BMT206]

A Clinical Study to Demonstrate Safety and Efficacy of E7777 (Denileukin Diftitox) in Persistent or Recurrent Cutaneous T-Cell Lymphoma [LYMNHL0103]