Welcome to the Winter 2013 issue of the Stanford Cancer Institute Clinical Research Newsletter! This quarterly publication is designed to inform our colleagues in the medical community about current clinical trials and research studies available at the Stanford Cancer Institute. Many of these trials provide access to novel therapies including new “targeted” agents, often not available in the community.

I would like to take this opportunity to share the news that Dr. George Sledge will be joining Stanford’s faculty in January 2013 as our next Chief of Medical Oncology. Dr. Sledge is a former president of the American Society for Clinical Oncology and a clinician-scientist at the Indiana University Simon Cancer Center, where he has focused on innovative treatments for breast cancer. Dr. Ron Levy, who has led our Medical Oncology program since 1993 will continue in his role as a leader of the Lymphoma research program.

For over 40 years, the researchers and clinicians in the Stanford Lymphoma Program have helped to define the standard of care for lymphomas, pioneering breakthrough immunotherapies and monoclonal antibodies, such as Rituximab. This program continues its groundbreaking work with its current clinical trials including a trial of a vaccine to treat mantle cell lymphoma and trials of targeted therapies.

The Stanford Hematology Program offers clinical trials and treatment regimens for patients with a variety of hematologic disorders. Multiple faculty physicians from Stanford’s Hematology program have been instrumental in improving patient survival and quality of life both locally and nationally through contributions to the prestigious National Comprehensive Cancer Network (NCCN) guidelines.

The clinical trials offered by the Stanford Blood and Marrow Transplant (BMT) Program ensure the smooth translation of its research findings into the most advanced patient care available today. Cross-disciplinary research into the molecular and genetic underpinnings of hematological disorders improves patient outcomes by translating clinical research into new treatments.

As always, the newsletter contains a listing of some of the Phase I and II trials from our Developmental Therapeutics Program. This program includes physician researchers in various areas of oncology, all interested in developing novel anticancer therapies.

We hope that you will consider the Stanford Cancer Center for one of our more than 300 clinical trials when you feel that it is appropriate to refer a patient to an academic medical facility. We, in turn, will make every effort to deliver great care to your patient, keep you informed of the patient’s treatment and response, and, if clinical trial treatment is not appropriate for your patient, return them to your care.

Sincerely,

Beverly S. Mitchell, MD
George E. Becker Professor of Medicine
Director, Stanford Cancer Institute
The Stanford Lymphoma Program is an international leader in lymphoma research offering a multidisciplinary, personalized approach to diagnostics and treatment for patients with Non-Hodgkin’s Lymphoma (NHL) and Hodgkin’s Disease (HD). For over 40 years Stanford researchers and clinicians have helped to define the standard of care for lymphomas worldwide, pioneering breakthrough immunotherapies and monoclonal antibodies and offering advanced treatments that are not yet available at other institutions. In addition, the program offers national cooperative group clinical trials that lead the integration of new drugs and imaging techniques into front-line therapy.

LEADING EDGE RESEARCH
Stanford Lymphoma Program members focus their research on lymphoma pathogenesis; diagnostic and therapeutic profiling of lymphoma subtypes; novel diagnostics and immunotherapeutics; Phase I and II clinical trials; cancer survivorship; and cutaneous lymphomas.

RESEARCH HIGHLIGHTS INVOLVE
• The discovery of Rituximab, a revolutionary lymphoma treatment and the best biological therapy available today to treat lymphoma. Stanford Cancer Institute researchers and physicians discovered the therapeutic effects of this monoclonal antibody and have been instrumental in developing its many applications. Some of the earliest Rituximab trials were carried out by Stanford physicians, with their patients having early access to this groundbreaking treatment.

• Continuing Innovation. Stanford lymphoma research focuses on:
  – A vaccine strategy to treat follicular NHL that is based on a combination of low dose radiation to one site of tumor and the injection of an immune stimulant directly into that same site. An immune response ensues against the tumor and attacks the tumor throughout the body.
  – An innovative clinical trial combining immunotherapy with hematopoietic stem cell transplantation for Mantle Cell Lymphoma.
  – Clinical trials of antibodies conjugated to a drug and directed against a target on lymphoma cells. One example is Brentuximab vedotin (now known as Adcetris) that is revolutionizing the treatment of recurrent Hodgkin’s Disease. Other such agents are under study for Non-Hodgkin’s Lymphoma.
  – Clinical trials of novel orally administered drugs that target the signaling molecules (BTK, SYC and PI3Kinase) inside lymphoma cells that are responsible for their uncontrolled growth.

• Cutaneous lymphoma research that includes:
  – Traditional therapies used more effectively. This has been exemplified by the modification of Stanford’s total skin electron beam therapy (TSEBT), known as the “Stanford TSEBT technique”, by reducing the total dose by two-thirds and combining with a potential radiation-enhancing systemic agent, such as a histone deacetylase inhibitor. This novel low-dose total skin electron beam therapy results in dramatic clearing of disease with significantly less toxicity.
  – A collaboration with genomics groups at Stanford to decipher the molecular mechanism of cutaneous lymphoma and discover new molecular targets for development of newer therapies.
  – Novel allogeneic HSCT regimen utilizing preparatory regimen of TSEBT, total lymphoid irradiation (TLI) and anthymocyte (ATG). 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 response has eluded systemic therapies.

• Genetics. Genome sequencing to more rapidly identify the unique mutations in each patient’s tumor. Recent identification of a set of two genes whose expression predicts survival in diffuse large B cell lymphoma (DLBCL), the most common form
of non-Hodgkin’s lymphoma. This new test identifies which patients need more aggressive therapy.

**TRANSLATIONAL RESEARCH: ADVANCED TREATMENT, CUSTOMIZED CARE**

The Lymphoma Program also includes an array of features demonstrating its dedication to translational research and customized care. Among these highlights are:

- Advanced therapies for NHL comprising:
  - Blood and marrow transplants
  - Immunotherapy
  - Experimental treatments through clinical trials

- Advanced treatments for HD focusing on:
  - A unique and highly curative chemotherapy/radiotherapy program known as Stanford V (five);
  - Biologic therapy development focusing on monoclonal antibodies and antibody-drug conjugates

- Innovative cutaneous lymphoma treatments and technologies
  - Targeted therapies that attack tumor surface proteins, aberrant epigenetic regulation, signaling or cell survival pathways, or microenvironment
  - Mogamulizumab (KW-0761), a bioengineered, humanized monoclonal antibody against CCR4, selectively expressed on tumor cells
  - Brentuximab vedotin, an antibody-drug-conjugate that targets CD30, commonly expressed on tumor cells in cutaneous T-cell lymphomas
  - 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
  - Pletalrexate, a newer anti-folate agent, combined with oral bexarotene demonstrates synergistic efficacy
  - Novel/newer topical agents including topical histone deacetylase inhibitor
  - Non-myeloablative allogeneic hematopoietic stem cell transplantation using total skin electron beam therapy, total lymphoid irradiation, and anti-thymocyte globulin 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

- Blood and marrow transplantation (BMT), with the single largest group of patients being treated with allogeneic or autologous marrow grafting. Among Stanford innovations is the non-myeloablative allogeneic transplant, an outpatient procedure with limited side effects and minimal need for hospitalization. Stanford researchers are also investigating the efficacy of vaccine therapy following BMT.

- A clinical database offering diagnostic results, treatment, and outcomes for more than 10,000 lymphoma and 5,000 Hodgkin’s Disease patients.

- New types of imaging that use new radiologic tracers for better delineation of disease.

- Multidisciplinary tumor boards, including a:
  - HD tumor board that meets weekly involving physicians from the Division of Oncology, and the Department of Radiation Oncology, along with radiologists and pathologists to review newly diagnosed, complex patients
  - Cutaneous lymphoma tumor board that meets weekly and is jointly directed by the Departments of Dermatology and Radiation Oncology

**A WORLD LEADER IN CUTANEOUS LYMPHOMA**

The Stanford Multidisciplinary Cutaneous Lymphoma Clinic (MCLC) is a leading center of excellence for clinical/translational research and treatment of patients with cutaneous lymphomas. In operation for over 30 years at Stanford, MCLC (tumor board) serves as a regional, national, and international referral center.

**MCLC FEATURES INCLUDE**

- A wide variety of clinical research protocols available for patient management, including biological skin-directed and systemic therapies such as immune stimulants, monoclonal antibodies, vaccines, new targeted agents, and novel radiation therapy strategies. Stanford leads efforts in therapeutic discoveries and FDA approval of new treatment options in cutaneous lymphoma.
Clinical Research Newsletter for Colleagues in the Community

Stanford Lymphoma Program continued

- Novel non-myeloablative allogeneic HSCT regimen for patients with mycosis fungoides and Sezary syndrome. This is offered as part of close collaboration and joint patient management with Stanford BMT faculty members and investigators.

- Leadership in patient-oriented, translational research with established collaboration with Stanford dermatology investigators who are world leaders in the study of genetic and epigenetic abnormalities in cutaneous malignancies.

STUDIES INCLUDE

Hodgkin’s Disease
- A Phase II Trial of Sequential SGN-35 Therapy with Adriamycin, Vinblastine, and Dacarbazine (S-AVD) for Older Patients with Untreated Hodgkin Lymphoma (LYMHD0009)
- Phase II Trial of Response-Adapted Therapy Based on Positron Emission Tomography (PET) for Bulky Stage I and II Classical Hodgkin Lymphoma (HL) (ECOGE2410)
- S0816, A Phase II Trial of Response-Adapted Therapy of Stage III-IV Hodgkin Lymphoma Using Early Interim FDG-PET Imaging (ECOGS0816)

Non-Hodgkin’s Lymphoma
- E2408, A 3-Arm Randomized Phase II Trial of Bendamustine-Rituximab (BR) Followed by Rituximab vs Bortezomib-BR (BVR) Followed by Rituximab vs BR Followed by Lenalidomide/Rituximab in High Risk Follicular Lymphoma (ECOGE2408)
- Phase I Study to Investigate the Safety and Clinical Activity of CAL-101 in Combination with Chemotherapeutic Agents and CD20 mAb in Patients with Relapsed or Refractory Indolent B-cell Non-Hodgkin’s Lymphoma, Mantle Cell Lymphoma or Chronic Lymphocytic Leukemia (HEM0017)
- A Phase II Study to Assess the Efficacy and Safety of CAL-101 in Patients with Indolent B-Cell Non-Hodgkin’s Lymphoma Refractory to Rituximab and Alkylating Agents (HEM0020)
- A Long-term Safety Study of Bruton’s Tyrosine Kinase (Btk) Inhibitor PCI-32765 in B cell Lymphoma and Chronic Lymphocytic Leukemia (LYMNHL0066-EX)
- A Randomized, Open-label, Dose-finding Study of Pralatrexate Plus Systemic Bexarotene in Patients with Relapsed or Refractory Cutaneous T-cell Lymphoma (LYMNHL0076)
- A Phase I, Open-label, Dose-finding Study of Low-dose (12 Gy) Total Skin Electron Beam Therapy (TSEBT) Combined with Vorinostat Versus Low-dose TSEBT Monotherapy in Mycosis Fungoides (MF) (LYMNHL0078)

- A Multicenter, Open-label, Randomized, Phase II Study Evaluating the Safety and Efficacy of Low-dose (12 Gy) Total Skin Electron Beam Therapy (TSEBT) Combined with Vorinostat Versus Low-dose TSEBT Monotherapy in Mycosis Fungoides (MF) (LYMNHL0089)
- Exploratory Pilot Study of Brentuximab Vedotin (SGN-35) in Patients with Mycosis Fungoides with Variable CD30 Expression Level (LYMNHL0089)

- A Randomized, Double-Blind, Placebo-controlled, Dose-Escalating Phase II Study to Assess the Safety, Pharmacodynamics and Pharmacokinetics of SHP-141, A Histone Deacetylase Inhibitor, Administered Topically Up to 28 Days to Patients with Stage IA, IB, or IIA Cutaneous T-Cell Lymphoma (LYMNHL0090)

- Phase II Study of a CpG-Activated Whole Cell Vaccine Followed by Autologous “Immunotransplant” for Mantle Cell Lymphoma (LYMNHL0040-BMT212)
- Rituximab/Bendamustine/Hydrochloride/Bortezomib + Rituximab & Lenalidomide in Mantle Cell Lymphoma [ECOG1411 25159]
- A Phase 2, Multicenter, Single-Arm Study to Evaluate the Efficacy and Safety of Single-Agent Bruton’s Tyrosine Kinase (BTK) Inhibitor, Ibrutinib, in Subjects with Mantle Cell Lymphoma Who Progress after Bortezomib Therapy (LYMNHL0098)
- A Phase II Study of Atorvastatin in Patients with Low Grade or Refractory Non-Hodgkin’s Lymphoma (Open Only to Marginal Zone Lymphoma or Chronic Lymphocytic Leukemia Patients) (LYMNHL0020)
- A Phase II Study of Cytoxan, Etoposide, Vincristine and Prednisone (CEOP) Alternating with Pralatrexate (P) as Front Line Therapy for Patients with Stage II, III and IV Peripheral T-Cell NHL (LYMNHL0094)
- A Phase II Study of Bruton’s Tyrosine Kinase (Btk) Inhibitor, PCI-32765, in Waldenstrom’s Macroglobulinemia (LYMWAL0006)
- A Phase I Study of PF-05082566 as a Single Agent in Patients with Advanced Cancer, and in Combination with Rituximab in Patients with Non-Hodgkin’s Lymphoma (NHL) (LYMNHL0092)
- A Phase II Study of Brentuximab Vedotin in Relapsed or Refractory CD30-Positive NHL (LYMNHL0093)
- A Phase I, Open-label, Dose-finding Study of Brentuximab Vedotin (SGN-35) in Patients with Mycosis Fungoides with Variable CD30 Expression Level (LYMNHL0078)
- A Randomized, Double-Blind, Placebo-controlled, Dose-Escalating Phase II Study to Assess the Safety, Pharmacodynamics and Pharmacokinetics of SHP-141, A Histone Deacetylase Inhibitor, Administered Topically Up to 28 Days to Patients with Stage IA, IB, or IIA Cutaneous T-Cell Lymphoma (LYMNHL0090)
- A Phase II Study of Atorvastatin in Patients with Low Grade or Refractory Non-Hodgkin’s Lymphoma (Open Only to Marginal Zone Lymphoma or Chronic Lymphocytic Leukemia Patients) (LYMNHL0020)
- FLT-PET/CT vs FDG-PETCT for Therapy Monitoring of Diffuse Large B-cell Lymphoma (LYMIMG0001)
Stanford Cancer Center’s Developmental Therapeutics Program, led by Branimir I. Sikic, MD, offers Phase I and II clinical trials using novel therapeutics. Dr. Sikic’s clinical interests are mainly in ovarian cancers and cancers of unknown primary. Other faculty participating in this effort include Drs. Heather Wakelee and Joel Neal (lung cancers), Dimitri Colevas (head and neck cancers), George Fisher and Pamela Kunz (GI cancers), Mark Pegram and Melinda Telli (breast cancers), Sunil Reddy (melanoma), and Ranjana Advani and Holbrook Kohrt (lymphomas).

As a translational clinical studies program, Developmental Therapeutics brings together outstanding physicians with internationally regarded scientists to develop novel therapies and diagnostic modalities that utilize cutting-edge science and technologies. This research focuses on early clinical studies, investigator-initiated trials, the development of analytic approaches to enhancing the discovery of drugs and targets, and the analysis of clinical trials.

Below is a sampling of currently available Phase I and II studies.

**PHASE I STUDIES**

**Multiple Solid Tumor Sites**
- A Phase I, Open-Label, Dose-Escalation Study of the Safety and Pharmacokinetics of MPDL3280A Administered Intravenously as a Single Agent to Patients with Locally Advanced or Metastatic Solid Tumors (VAR0082)
- A Phase I, Open-label, Dose-escalation, Safety and Pharmacokinetic Study of CDX-1127 in Patients with Selected Refractory or Relapsed Hematologic Malignancies or Solid Tumors (VAR0081)
- A Phase I, Open-Label, Dose-Escalation Study of the Safety, Tolerability, Pharmacokinetics and Immunoregulatory Activity of BMS-663513 (Anti-CD137) in Subjects with Advanced and/or Metastatic Solid Tumors (VAR0071)

**Lymphomas**
- A Phase I Study of PF-05082566 as a Single Agent in Patients with Advanced Cancer, and in Combination with Rituximab in Patients with Non-Hodgkin’s Lymphoma (NHL) (LYMNHL0082)

**PHASE II STUDIES**

**Thymic Cancers**
- A Phase II Study of Amrubicin in Relapsed or Refractory Thymic Malignancies (THOR0003)

**Gastric Cancers**
- A Phase II Study of Capecitabine, Carboplatin, and Bevacizumab for Metastatic or Unresectable Gastroesophageal Junction and Gastric Adenocarcinoma (GI0002)

**Lymphoma**
- A Randomized, Open-Label, Multicenter, Phase II Trial Evaluating the Safety and Activity of DCDT2980S in Combination with Rituximab or DCD84501A in Combination with Rituximab in Patients with Relapsed or Refractory B-Cell Non-Hodgkin’s Lymphoma (Opening to Enrollment Early 2013)
The Stanford Blood and Marrow Transplant (BMT) program is a nationally recognized authority in BMT research, and the largest BMT program in Northern California. Stanford BMT clinical trials ensure the smooth translation of research findings into the most advanced patient care available today. For more than 25 years, with its cutting edge medicine, excellent long-term follow up care of patients, and multidisciplinary team of specialists, the BMT Program treats patients from around the world with a variety of malignant and non-malignant diseases, including lymphoma, myeloma, leukemia, myelodysplastic syndrome, and selected solid tumors.

**Stanford BMT Research Discoveries, New Therapies with Global Impact**
In addition to successful clinical practice, Stanford BMT researchers are converting their discoveries into new therapies, advancing the efficacy of hematopoietic cell transplantation for patients worldwide.

The BMT Program supports cross-disciplinary research into the molecular and genetic underpinnings of hematological disorders, improving patient outcomes by translating clinical research into new treatments. In collaboration with the Center for Clinical Immunology at Stanford, the program is developing new ways to boost the immune tolerance of transplanted blood or marrow-derived stem cells. Furthermore, its state-of-the-art laboratory is exploring novel cellular and vaccine-based therapies that target hematologic disease at its most basic origins.

**Stanford BMT Cutting Edge Research Focuses On**
- Cellular Therapeutics – translational research investigating specific cell populations, such as regulatory T-cells, cytokine induced killer (CIK) cells, tumor vaccines, and memory T-cells.
- Investigations of novel approaches to the prevention and treatment of Graft-vs.-host disease (GVHD).
- Haploidentical hematopoietic cell transplantation.
- Novel TLI/ATG allogeneic preparative regimen that reduces rates of GVHD and lowers transplant-related risks in select disease types.

**Stanford BMT – Distinct Features**
The BMT program has been very successful with a history of limited morbidity rates and acute mortality that is well below most published reports. Some of its many highlights include:

- Inpatient and Outpatient Transplants.
  - Stanford has expertise in managing all transplant types—autologous, allogeneic-related donor and allogeneic-unrelated donor—and in handling the most complicated cases.
  - Stanford has provided transplants to more than 4500 adult patients and performs over 300 transplants annually, with almost one-half performed in its outpatient Infusion Treatment Area with no scheduled inpatient admission.
  - Stanford has a dedicated 22-bed inpatient BMT unit, staffed by nurses who specialize in the care of BMT patients. All rooms are equipped with special HEPA filtration systems.
• Physician Expertise.
  – Nine physicians focus exclusively on BMT with a dedicated Immunocompromised Host Infectious Disease service.
  – Patient follow up occurs over the long-term to provide support and consultation and to accurately reflect long-term outcomes, with ongoing tracking of over 90% of patients.

• Dedicated BMT Laboratory. Specialties include:
  – Good Tissue Practice/Good Manufacturing Practice processing capabilities and state-of-the-art technologies
  – High speed cell sorting holding great promise for future treatment and prevention of graft-vs.-host disease (GVHD).

• FACT Accreditation. Stanford’s BMT program is fully accredited by the Foundation for the Accreditation of Cellular Therapy (FACT) and is a member of the BMT Clinical Trials network.

• National Marrow Donor Program (NMDP) accredited transplant center, apheresis center, and collection center. Stanford’s Blood and Marrow Transplant group was recently recognized by the National Marrow Donor Program for collecting over 250 peripheral blood stem cell collections for marrow transplant. Since its start in 1987, the Stanford BMT team has collected over 400 donations. BMT also received special recognition for excellence in performance surrounding donor care, product integrity, data submission, and overall service.

• Community Involvement. Faculty and Staff collaborate with patients, their families, and the medical community by contributing to the global discussion on key biomedical and technological issues shaping the future of blood and marrow transplantation. This includes:
  – Regularly conducting educational seminars for participants in the Leukemia and Lymphoma Society’s Team in Training, American Cancer Society, the Bay Area Multiple Myeloma Support Group, the Fattal Foundation, and medical audiences at community hospitals and Grand Rounds across the country.
  – Actively participating in the American Society of Blood and Bone Marrow Transplantation, the American Society of Hematology, and other organizations.

STUDIES INCLUDE

• Allogeneic Hematopoietic Cell Transplantation Using a Non-Myeloablative Preparative Regimen of Total Lymphoid Irradiation and Anti-Thymocyte Globulin for Older Patients with Hematologic Malignancies (BMT153)

• Total Lymphoid Irradiation and Anti-Thymocyte Globuline as Conditioning for Non-Myeloablative Allogeneic Hematopoietic Cell Transplantation for the Treatment of Myelodysplastic Syndromes and Myeloproliferative Disorders (except CML) (BMT168)

• Autologous Followed by Non-myeloablative Allogeneic Transplantation for Non-Hodgkin’s Lymphoma (BMT185)

• A California Cooperative Clinical Study Comparing Allogeneic Hematopoietic Cell Transplantation Using Nonmyeloablative Host Conditioning with Total Lymphoid Irradiation and Anti-thymocyte Globulin versus Best Standard of Care in Acute Myeloid Leukemia(AML) in First Complete Remission (BMT190)

• Defibrotide for Hematopoietic Stem Cell Transplant (SCT) Patient with Severe Hepatic Veno-occlusive Disease (VOD): A Treatment IND Study (BMT196)

• A Multicenter Phase I/II Study of the Prophylactic Inhibition of BCR-ABL Tyrosine Kinase by Tasigna® (Nilotinib) after

• highlighted studies are Stanford investigator initiated
Hematopoietic Cell Transplantation for Philadelphia Chromosome-Positive Leukemias (BMT202)

- Randomized Placebo Controlled Double Blind Study of Restasis versus Placebo in Primary Prevention of Ocular GVHD after Allogeneic Stem Cell Transplantation (BMT205)

- 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 Randomized Phase II Study of Imatinib and Rituximab for Cutaneous Sclerosis after Allogeneic Hematopoietic Cell Transplantation (BMT211)

- A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma (BMT213)

- Post Transplant Infusion of Allogeneic Cytokine Induced Killer Cells as Consolidate Therapy after Non-Myeloablative Allogeneic Transplantation in Patients with Myelodyplasia or Myeloproliferative Disorders (BMT217)

- A Phase I Study of Nilotinib in Steroid Dependent / Refractory Chronic Graft versus Host Disease (BMT222)

- A Phase III, Double-Blind, Randomized, Placebo-Controlled, Multi-center Clinical Trial to Study the Safety, Tolerability, Efficacy, and Immunogenicity of V212 in Recipients of Autologous Hematopoietic Cell Transplants (HCTs) (BMT226)

- Longitudinal Study of Immune Mediated Disorders after Allogeneic HCT Protocol (BMT227)

- A Randomized, Placebo-controlled, Multi-site Phase II Study Evaluating the Safety and Efficacy of Preemptive Treatment with CMX0001 for the Prevention of Adenovirus Disease Following Hematopoietic Stem Cell Transplantation (The ADV HALT TRIAL) (BMT231)

- Phase III, Double Blind, Randomized Study to Evaluate Safety and Efficacy of BAL8557 versus Voriconazole for Primary Treatment of Invasive Fungal Disease Caused by Aspergillus Species or Other Filamentous Fungi (BMT233)

- Intratumoral Injection of an Immunostimulatory CpG, SD-101, Combined with Local Radiation for the Treatment of Recurrent or Progressive Lymphoma after Allogeneic Hematopoietic Cell Transplantation (BMT235)

- Phase II/III Trial for Patients with Advanced Hematologic Malignancies Undergoing Myeloablative Allogeneic HCT with a T cell Depleted Graft with Simultaneous Infusion of Conventional T Cells and Regulatory T Cells (BMT236)

- An Open Label Study of Isavuconazole in the Treatment of Patients with Aspergillosis and Renal Impairment or of Patients with Invasive Fungal Disease Caused by Rare Molds, Yeasts or Dimorphic Fungi. WSA-CS-003 (BMT238Z)

- A Phase III, Double-Blind, Randomized Study to Evaluate the Safety and Efficacy of BAL8557 versus a Caspofungin Regimen in the Treatment of Candidemia and Other Invasive Candida Infections (BMT239U)

- A Randomized, Prospective, Double Blind, Placebo Controlled, Phase III Study of US-ATG-F Prophylaxis as a Supplement to Standard of Care Prophylaxis to Prevent Moderate to Severe Chronic GVHD in Adult Acute Myeloid Leukemia, Acute Lymphoid Leukemia, and Myelodysplastic Syndrome Patients after Allogeneic Stem Cell Transplantation From Unrelated Donors (BMT240)

- Early Behavioral Intervention in BMT Recipients with Sleep Disturbance: Assessing Its Impact on Quality of Life, Fatigue and Cognitive Function (BMT242)

- A Phase I Study of CD8+ Memory T-Cell Donor Lymphocyte Infusion for Relapse of Hematolymphoid Malignancies Following Matched Related Donor Allogeneic Hematopoietic Cell Transplantation (BMT243)

- Targeted Therapy of Bronchiolitis Obliterans Syndrome (BOS) (BMT244)

- A Phase II/III Randomized, Multicenter Trial Comparing Sirolimus plus Prednisone and Sirolimus/Calcineurin Inhibitor plus Prednisone for the Treatment of Chronic Graft-versus-Host Disease (BMT245)

- highlighted studies are Stanford investigator initiated

Clinical Research Newsletter for Colleagues in the Community
The Stanford Hematology Program features a leading edge research program and offers state-of-the-art diagnostics and treatment regimens for patients with a variety of hematologic disorders, including acute and chronic leukemias (ALL, AML, CLL, CML), multiple myeloma, amyloidosis, myelodysplastic syndromes, and myeloproliferative disorders. Collaborative, translational research programs at Stanford have led to innovative therapies for many of these diseases. Stanford faculty physicians have also been instrumental in improving patient survival and quality of life both locally and nationally through their contributions to the prestigious National Comprehensive Cancer Network (NCCN) guidelines that are widely used for the management of hematologic malignancies.

The Hematology Program includes a comprehensive team of specialists who focus exclusively on both benign and malignant hematologic disorders. They work in close collaboration with Stanford physician specialists in Blood and Marrow Transplantation and other disciplines including infectious diseases, pathology, radiation oncology, and interventional radiology. They are also leaders in SWOG, one of the three national cooperative groups that conducts clinical trials for patients with cancer.

**LEADING THERAPEUTIC RESEARCH**
The Stanford Hematology Program’s clinical investigators and laboratory scientists are focused on developing novel treatments for a wide variety of hematological disorders.

**RESEARCH HIGHLIGHTS FEATURE**

- **Innovative Treatments and Technologies.** Stanford researchers are advancing new cancer treatments not yet commercially available, including:
  - Novel investigational therapeutics that are at all stages of development, from early phase I trials to randomized phase III studies.
  - Minimally invasive spine surgery for multiple myeloma patients.
  - New molecular imaging modalities for diagnostic purposes and to assess response to treatment.

- **Cutting Edge Translational Research.** Stanford Hematology is at the leading edge of translational research, offering clinical trials for all types of hematologic malignancies. Clinical trials involving new agents, including targeted therapies, are the backbone of the program, which focuses on:
  - Development of novel therapeutic strategies for elderly patients with leukemia, particularly AML and CLL.
  - A multidisciplinary approach to the treatment of myelodysplastic syndromes, multiple myeloma, and amyloidosis.
  - Targeted, oral therapies for myelofibrosis patients.
  - Incorporation of molecular markers to aid in prognosis, guide therapy, and monitor for disease recurrence.
  - Oral, targeted therapy for chronic lymphocytic leukemia including the investigational agents CAL-101 (GS1101) and ibrutinib.
  - Arsenic trioxide for acute promyelocytic leukemia.

- **Genetic Research.** Stanford investigators are defining the biologic mechanisms responsible for the development of leukemia, and creating more effective therapies to address these diseases. This research includes:
  - Identification of a set of 133 genes that point to the most dangerous subtypes of AML. In the not so distant future, this research may help physicians select the best treatment for their AML patients.
  - Investigation of genetic profiles, including whole genome sequencing that can help doctors make better decisions in treating CLL.
  - Monitoring minimal residual disease in ALL to identify patients at risk for relapse.
  - Development of leukemia stem cell-specific markers and targeted therapies.
STUDIES INCLUDE

**Leukemia**

*Multiple Histologies*

- An Open-Label, Dose Escalation, Phase I Study of MLN4924, a Novel Inhibitor of Nedd8-Activating Enzyme, in Adult Patients with Acute Myelogenous Leukemia, High-Grade Myelodysplastic Syndrome, and Acute Lymphoblastic Leukemia (HEM0011)

- A Phase I/II Trial of CLT-008 Myeloid Progenitor Cells in Patients Receiving Post-Remission Therapy for High Risk Leukemia or Myelodysplasia (MDS) (HEM0019)

- An Open-Label, Multicenter, Phase I Trial of the Safety and Pharmacokinetics of Escalating Doses of DCDT2980S in Patients with Relapsed or Refractory B-Cell Non-Hodgkin’s Lymphoma and Chronic Lymphocytic Leukemia (Open to NHL, SLL, DLBCL, MCL or CLL Patients) (VAR0059)

**Acute Lymphoblastic Leukemia (ALL)**

- An Open-Label, Phase I Study of Inotuzumab Ozogamicin in Subjects with Relapsed or Refractory CD22-Positive Acute Lymphocytic Leukemia (HEMALL0007)

- Phase II Study of Combination of Hyper-CVAD and Dasatinib (NSC-732517) with or without Allogeneic Stem Cell Transplant in Patients with Philadelphia (Ph) Chromosome Positive and/or Bcr-Abl Positive Acute Lymphoblastic Leukemia (ALL) (SWOGS0805)

**Acute Myeloid Leukemia (AML)**

- An Open-Label, Dose Escalation, Phase I Study of MLN4924, a Novel Inhibitor of Nedd8-Activating Enzyme, in Adult Patients with Acute Myelogenous Leukemia, High-Grade Myelodysplastic Syndrome, and Acute Lymphoblastic Leukemia (HEM0011)

- Phase II Study of Clofarabine with High Dose Cytarabine and G-CSF Priming in Adult Patients Less than Age 65 with Newly Diagnosed Acute Myeloid Leukemia or Advanced Myelodysplastic Syndrome and/or Advanced Myeloproliferative Neoplasm (HEM0018)

- A Phase Ib, Dose-Finding Study of Oral Panobinostat (LBH589) in Combination with Idarubicin and Cytarabine Induction and High-Dose Cytarabine-Based Consolidation Therapy in Adult Patients Less than 65 Years Old with Acute Myeloid Leukemia (AML) (HEMAML0015)

- A Phase II, Multicenter, Randomized, Open-Label, Parallel-Group Study of a Lenolidomide (Revlimid®) Regimen or a Sequential Azacitidine (Vidaza®) Plus Lenolidomide (Revlimid®) Regimen Versus an Azacitidine (Vidaza®) Regimen for Therapy of Older Subjects with Newly Diagnosed Acute Myeloid Leukemia (HEMAML0016)

- A California Cooperative Clinical Study Comparing Allogeneic Hematopoietic Cell Transplantation Using Nonmyeloablative Host Conditioning with Total Lymphoid Irradiation and Anti-thymocyte Globulin versus Best Standard of Care in Acute Myeloid Leukemia (AML) in First Complete Remission (BMT190)

**Acute Promyelocytic Leukemia (APL)**

- A Phase II Study of ATRA, Arsenic Trioxide and Gemtuzumab Ozogamicin in Patients with Previously Untreated High-Risk Acute Promyelocytic Leukemia (SWOGS0535)

**Chronic Lymphocytic Leukemia (CLL)**

- A Randomized, Multicenter, Open-label, Phase III Study of the Bruton’s Tyrosine Kinase (BTK) Inhibitor Ibrutinib versus Ofatumumab in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (HEM0025)

- A Phase I Study to Investigate the Safety and Clinical Activity of CAL-101 in Combination with Chemotherapeutic Agents and Anti-CD20 mAb in Patients with Relapsed or Refractory Indolent B-cell Non-Hodgkin’s Lymphoma, Mantle Cell Lymphoma or Chronic Lymphocytic Leukemia (HEM0017)

- A Phase II Single Arm Study to Investigate the Safety and Clinical Activity of CAL-101 in Combination with Rixtuximab in Elderly Patients with Previously Untreated Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma (HEM0021)

- A Phase III, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of GS-1101 (CAL-101) in Combination with Rixtuximab for Previously Treated Chronic Lymphocytic Leukemia (HEMCLL0012)

- A Phase III, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of GS-1101 (CAL-101) in Combination with Bendamustine and Rixtuximab for Previously Treated Chronic Lymphocytic Leukemia (HEMCLL0013)
• An Open-Label, Multicenter, Phase I Trial of the Safety and Pharmacokinetics of Escalating Doses of DCDS4501A in Patients with Relapsed or Refractory B-Cell Non-Hodgkin’s Lymphoma and Chronic Lymphocytic Leukemia (VAR0068)

**Multiple Myeloma and Amyloidosis**

• A Phase I Study of Bortezomib (VELCADE) in Combination with Pralatrexate in Relapsed/Refractory Multiple Myeloma (HEMMYL0014)

• A Phase I/II Study of Amrubicin in Combination with Lenalidomide and Weekly Dexamethasone in Relapsed/Refractory Multiple Myeloma (HEMMYL0018)

• An Open-Label, Dose-Escalation, Phase I/II Study of the Oral Formulation of MLN9708 Administered Twice-weekly in Combination with Lenalidomide and Dexamethasone in Patients with Newly Diagnosed Multiple Myeloma Requiring Systemic Treatment (HEMMYL0019)

**Myelodysplastic Syndrome (MDS)**

• Phase II Study of Clofarabine with High Dose Cytarabine and G-CSF Priming in Adult Patients Less Than Age 65 With Newly Diagnosed Acute Myeloid Leukemia or Advanced Myelodysplastic Syndrome and/or Advanced Myeloproliferative Neoplasm (HEM0018)

• A Phase I/II Trial of CLT-008 Myeloid Progenitor Cells in Patients Receiving Post-Remission Therapy for High Risk Leukemia or Myelodysplasia (MDS) (HEM0019)

• Azacitidine Plus Lenalidomide Combination in Elderly Patients with Previously Treated AML and High-Risk MDS (VIREL2 Trial) (HEMO022)

• A Pilot Study of Lenalidomide in Adult Diamond-Blackfan Anemia Patients with Red Blood Cell Transfusion-Dependent Anemia (HEMMDS0022)

• A Phase III, Multi-Center, Randomized, Controlled Study to Assess the Efficacy and Safety of ON 01910.Na Administered as a 72-Hour Continuous Intravenous Infusion Every Other Week in Myelodysplastic Syndrome Patients with Excess Blasts Relapsing After, or Refractory to, or Intolerant to Azacitidine or Decitabine (HEMMDS0026)]

• Total Lymphoid Irradiation and Anti-Thymocyte Globuline as Conditioning for Non-Myeloablative Allogeneic Hematopoietic Cell Transplantation for the Treatment of Myelodysplastic Syndromes and Myeloproliferative Disorders (except CML) (BMT168)

• Post Transplant Infusion of Allogeneic Cytokine Induced Killer Cells as Consolidate Therapy after Non-Myeloablative Allogeneic Transplantation in Patients with Myelodysplasia or Myeloproliferative Disorders (BMT217)

**Myeloproliferative Disorders (MPD)**

• Phase II Study of Clofarabine with High Dose Cytarabine and G-CSF Priming in Adult Patients Less Than Age 65 with Newly Diagnosed Acute Myeloid Leukemia or Advanced Myelodysplastic Syndrome and/or Advanced Myeloproliferative Neoplasm (HEM0018)

• A Single Arm, Phase II, Open-label Study to Determine the Efficacy of 100mg Twice Daily Oral Dosing of Midostaurin Administered to Patients with Aggressive Systemic Mastocytosis or Mast Cell Leukemia +/- an Associated Hematological Clonal Non-Mast Cell Lineage Disease (HEMMPD0007)

• A Phase II Study to Evaluate the Efficacy and Safety of GS-6624 in Adult Subjects with Primary, Post Polycythemia Vera or Post Essential Thrombocythemia Myelofibrosis (HEMMPD0013)

• A Phase III, Multicenter, Randomized, Double-blind, Placebo-controlled, 3-Arm Study of SAR302503 in Patients with Intermediate-2 or High-risk Primary Myelofibrosis, Post-polycythemia Vera Myelofibrosis, or Post-essential Thrombocythemia Myelofibrosis with Splenomegaly (HEMMPD0015)

• Total Lymphoid Irradiation and Anti-Thymocyte Globuline as Conditioning for Non-Myeloablative Allogeneic Hematopoietic Cell Transplantation for the Treatment of Myelodysplastic Syndromes and Myeloproliferative Disorders (except CML) (BMT168)

• Post Transplant Infusion of Allogeneic Cytokine Induced Killer Cells as Consolidate Therapy after Non-Myeloablative Allogeneic Transplantation in Patients with Myelodysplasia or Myeloproliferative Disorders (BMT217)

• highlighted studies are Stanford investigator initiated