HEMATOLOGIC ONCOLOGY

2014 ANNUAL REPORT

Memorial Sloan Kettering Cancer Center

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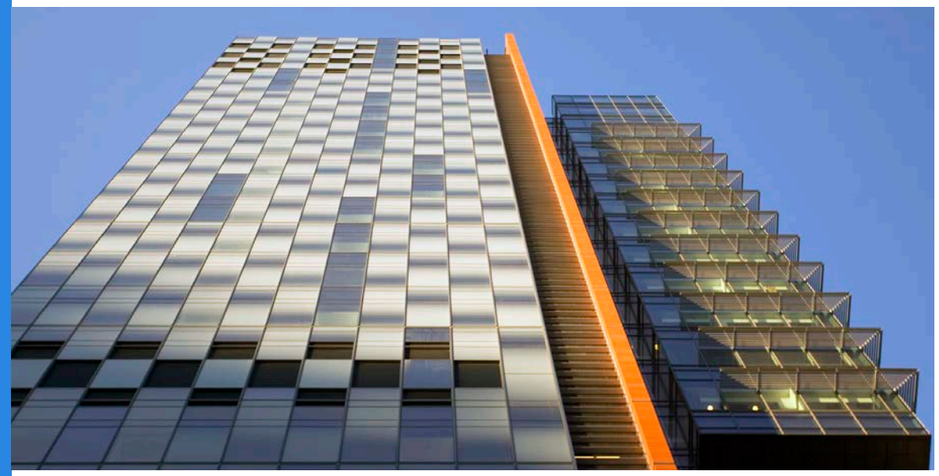
MSK'S REGIONAL NETWORK: (LEFT TO RIGHT)
TOP ROW: MEMORIAL HOSPITAL; MIDDLE ROW: MSK ROCKVILLE CENTER, MSK WEST HARRISON; BOTTOM ROW: MSK 74TH STREET, MSK BASKING RIDGE

ON THE COVER: (LEFT TO RIGHT) GERALD SOFF, NEHA KORDE, ALEENA ASLAM, JEANETTE BOUDREAU, KATHARINE HSU, MARTIN TALLMAN, STEVEN HORWITZ

Letter from the Division Head



ZUCKERMAN RESEARCH CENTER

THE DIVISION OF HEMATOLOGIC ONCOLOGY continues to grow and we welcomed four new faculty members in 2014, including Dr. Ola Landgren, Chief Attending of the Myeloma Service. The Division is now home to 60 faculty members in 5 services, who are all devoted to clinical care, research and education for patients with a hematological malignancy.

The use of a patient's own T cells programmed to eliminate tumor cells through the expression of a chimeric antigen receptor (CAR) has shown remarkable activity in patients with acute lymphoblastic leukemia and in late 2014, the US Food and Drug Administration granted MSK Breakthrough Therapy Designation for this therapy.

Basic research from several laboratories at our center played an important role in the development of a drug that can inhibit an enzyme resulting from a mutated gene that encodes IDH2, a protein that is normally involved in the generation of energy within the cell. The early results of this drug show promising effects in patients with hematological malignancies carrying the mutated IDH2 gene.

MSK continues its efforts to treat patients closer to home in the outpatient facilities of its regional network. Several physicians in the Division have their primary practice in these facilities and are dedicated to bringing the same standard of care for patients with hematological malignancies throughout the network. In October 2014, MSK opened a new outpatient facility in West Harrison and several of our physicians have opened a practice at this site.

These are just a few of the exciting accomplishments of our Division, which are highlighted in this 4th edition of our Annual Report.

Best regards,

MARCEL R.M. VAN DEN BRINK, MD, PHD
ALAN HOUGHTON CHAIR IN IMMUNOLOGY
HEAD, DIVISION OF HEMATOLOGIC ONCOLOGY
MEMORIAL SLOAN KETTERING CANCER CENTER

Division of Hematologic Oncology Faculty

ADULT BONE MARROW TRANSPLANTATION


Juliet Barker


Hugo Castro-Malaspina


David Chung


Parastoo Dahi


Sergio Giralt
CHIEF ATTENDING


Boglarka Gyurkocza


Alan Hanash


Katharine Hsu


Ann Jakubowski


Robert Jenq


Guenther Koehne

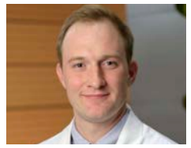

Heather Landau


Esperanza Papadopoulos


Miguel Perales


Doris Ponce


Craig Sauter


Brian Shaffer


Roni Tamari

HEMATOLOGY


Marcel van den Brink
DIVISION HEAD


James Young


Simon Mantha


Rekha Parameswaran


Lilian Reich

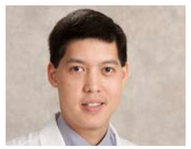

Gerald Soff
CHIEF ATTENDING

LEUKEMIA


Omar Abdel-Wahab


Ellin Berman


Renier Brentjens


Stephen Chung


Bayard Clarkson


Dan Douer


Virginia Klimek


Ross Levine

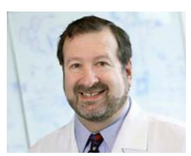

Peter Maslak

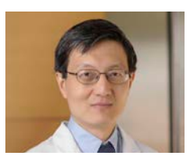

Michael Mauro†

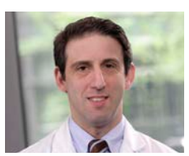

Jae Park


Raajit Rampal

LYMPHOMA


David Scheinberg


Alan Shih


Eytan Stein


Martin Tallman
CHIEF ATTENDING

Helen Chung

John Gerecitano

Paul Hamlin†
CHIEF, BASKING RIDGE
MEDICAL ONCOLOGY SERVICE

Steven Horwitz

Anita Kumar*

Matthew Matasar†

Alison Moskowitz

Craig Moskowitz
CLINICAL DIRECTOR

Ariela Noy

Lia Palomba

Carol Portlock

David Straus

Elina Tsyvkin*

Anas Younes
CHIEF ATTENDING

MYELOMA

Andrew Zelenetz†

Hani Hassoun†

Neha Korde*

Ola Landgren*
CHIEF ATTENDING

Nikoletta Lendvai

Alexander Lesokhin

REGIONAL NETWORK

Philip C. Caron

Pamela R. Drullinsky

Audrey M. Hamilton

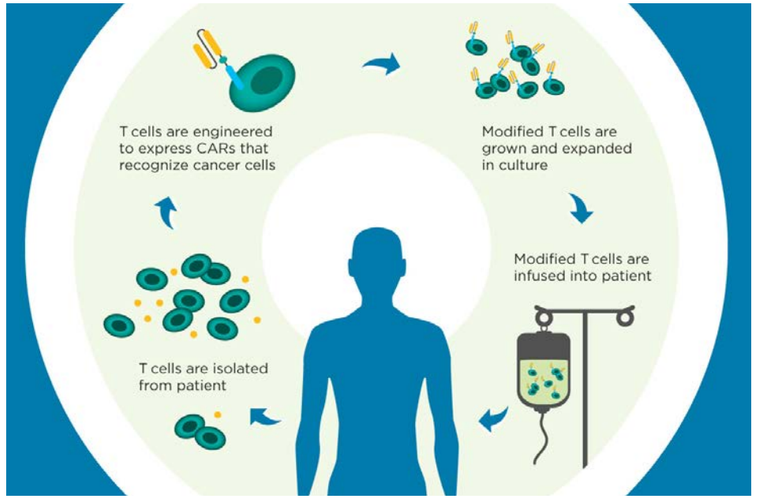
COLLABORATING TEAMS

- Cardiology Service
- Case Management
- Colorectal Service
- Critical Care Medicine Service
- Dental Service
- Dermatology Service
- Endocrinology Service
- Gastroenterology and Nutrition Service
- Gastric and Mixed Tumor Service
- General Internal Medicine Service
- Geriatrics Service
- Gynecology Service
- Head and Neck Service
- Hepatopancreatobiliary Service
- Infectious Diseases Service
- Integrative Medicine Service
- Interventional Radiology Service
- Music/Art Therapy
- Neurology Service
- Neurosurgery
- Nursing
- Nutrition
- Occupational Therapy
- Ophthalmic Oncology Service
- Orthopaedic Service
- Pain and Palliative Care Service
- Pathology
- Diagnostic Molecular Pathology
- Hematopathology
- Pathology Diagnostic Services, Cytology
- Surgical Pathology Diagnostic Services
  - Bone and Soft Tissue Pathology
  - Dermatopathology
  - Gastrointestinal Pathology
- Physical Therapy
- Plastic and Reconstructive Surgical Service
- Psychiatry Service
- Pulmonary Service
- Radiation Oncology
- Radiology
- Rehabilitation Medicine Service
- Renal Service
- Social Work
- Surgery
- Thoracic Service
- Urgent Care Center
- Urology Service

*JOINED FACULTY IN 2014
† PHYSICIANS WHO ALSO PRACTICE IN THE REGIONAL NETWORK

“Living Therapies” Developed at MSK Provide New Approach for Cancer Treatment

Cell therapies, a promising new type of cancer treatment, aim to boost the immune system by giving immune cells the information they need to better recognize tumor cells as foreign and attack them. These therapies are being used to treat a few types of cancer, with more trials planned.



T CELL IMMUNOTHERAPY INVOLVES ENGINEERING A PATIENT’S OWN CELLS TO RECOGNIZE A PROTEIN PRESENT IN CANCER CELLS, ENABLING THEM TO SEEK OUT AND DESTROY THE CANCER.

WHEN PEOPLE THINK of treatments for cancer, they likely think of surgery, radiation therapy, and drugs — both traditional chemotherapy and, more recently, targeted drugs. Increasingly, however, cancer therapies may be vaccines, antibodies, or therapies made from whole cells.

Cell therapies, sometimes called “living therapies,” are an especially promising and rapidly growing area of cancer research. One approach that’s been pioneered by Memorial Sloan Kettering researchers, led by investigator Michel Sadelain, is called CAR T cell immunotherapy. This type of targeted immunotherapy aims to boost the immune system by giving immune cells the information they need to better recognize tumor cells as foreign and attack them.

MSK investigator Michel Sadelain coined the term “living therapies.”

The technique involves filtering white blood cells called T cells from a patient’s blood and introducing a new gene into those cells. A disabled virus called a vector is used to carry the gene inside the T cells and insert it into the cells’ genomes.

The gene programs the T cells to make a chimeric antigen receptor (CAR), which enables them to recognize a specific protein that’s present in cancer cells. The CAR T cells are then grown in the laboratory and infused back into the patient, where they seek out and destroy the cancer.

CAR T cells help the immune system to recognize and destroy cancer cells.

CAR T cell therapy is currently being evaluated in the clinic at MSK for certain types of leukemia and lymphoma. In this approach, T cells are genetically engineered to recognize a protein called CD19, which is found on the surface of blood cells called B cells. In the largest study reported so far, for adult patients with B cell acute lymphoblastic leukemia — a rapidly progressing form of blood cancer — a report published by MSK researchers last year found that 88 percent of patients responded to the therapy. In late 2014, the US Food and Drug Administration granted MSK Breakthrough Therapy Designation for its CD19 CAR therapy.

CAR therapy is also currently being studied at MSK for the treatment of a type of sarcoma (a cancer of the soft tissues) as well as advanced prostate cancer that has stopped responding to other treatments. Plans are under way to begin trials for other kinds of cancer as well, including tumors of the chest cavity — mesothelioma and certain lung and breast cancers — and ovarian cancer.

HIGHLIGHTS

- CAR T cell therapy was first developed at MSK.
- A chimeric antigen receptor (CAR) helps T cells identify tumors.
- These T cells then recognize tumors as foreign and attack them.
- CAR T cell therapy is being used to treat leukemia and other cancers.

OVER THE PAST DECADE, DRS. RENIER BRENTJENS, ISABELLA RIVIÉRE, AND MICHEL SADELAIN HAVE INVESTIGATED AN APPROACH THAT INVOLVES REMOVING WHITE BLOOD CELLS CALLED T CELLS FROM PATIENTS AND INTRODUCING A NEW GENE INTO THE CELLS USING AN ENGINEERED VIRAL VECTOR.

CAR T CELL THERAPY: Open Therapeutic Clinical Trials

A Phase I Clinical Trial of Malignant Pleural Disease Treated with Autologous T Cells Genetically Engineered to Target the Cancer-Cell Surface Antigen Mesothelin
IRB 15-007, PI: Prasad Adusumilli

A Phase I Clinical Trial for the Treatment of ß-Thalassemia Major with Autologous CD34+ Hematopoietic Progenitor Cells Transduced with TNS9.3.55, a Lentiviral Vector Encoding the Normal Human ß-Globin Gene
IRB 10-164, PI: Farid Boulad

A Phase I Dose Escalation Trial Using In Vitro Expanded Allogeneic Epstein-Barr Virus Specific Cytotoxic T-Lymphocytes (EBV-CTLs) Genetically Targeted to the B-Cell Specific Antigen CD19 Positive Residual Or Relapsed Acute Lymphoblastic Leukemia After Allogeneic Hematopoietic Progenitor Cell Transplantation
IRB 11-038, PI: Kevin Curran

A Phase I Trial of Autologous T-Lymphocytes Genetically Targeted to the B-Cell Specific Antigen CD19 in Pediatric and Young Adult Patients with relapsed B-Cell Acute Lymphoblastic Leukemia
IRB 13-052, PI: Kevin Curran

A Phase I/IIa Trial For The Treatment of Relapsed or Chemotherapy Refractory Chronic Lymphocytic Leukemia or Indolent B Cell Lymphoma Using Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19
IRB 06-138, PI: Jae Park

A Phase I Trial of Precursor B Cell Acute Lymphoblastic Leukemia (B-ALL) Treated with Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19(CAR)
IRB 09-114, PI: Jae Park

A Phase I Trial of Consolidation Therapy with Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19 in Patients with Chronic Lymphocytic Leukemia Following Upfront Chemotherapy with Pentostatin, Cyclophosphamide and Rituximab
IRB 11-048, PI: Jae Park

The ROCKET Study: A Phase II, Single-arm, Multicenter Trial to Determine the Efficacy and Safety of JCAR2015 in Adult Subjects with Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia
IRB 15-099, PI: Jae Park

A Phase I Trial of High Dose Therapy and Autologous Stem Cell Transplantation Followed by Infusion of Chimeric Antigen Receptor (CAR) Modified T-Cells Directed Against CD19+ B-Cells for Relapsed and Refractory Aggressive B Cell Non-Hodgkin Lymphoma
IRB 12-117, PI: Craig Sauter

Adoptive Transfer of Autologous T Cells Targeted to Prostate Specific Membrane Antigen (PSMA) for the Treatment of Castrate Metastatic Prostate Cancer (CMPC)
IRB 09-036, PI: Susan Slovin

Why I Would Refer a Lymphoma Patient to Memorial Sloan Kettering

ANAS YOUNES, MD

I CAN THINK of many reasons to refer a patient with newly diagnosed or relapsed/refractory Hodgkin or non-Hodgkin lymphoma to Memorial Sloan Kettering. But my top five are these:

OUR EXTENSIVE EXPERIENCE

The collective knowledge of our lymphoma experts is unparalleled around the globe. Many of our 12 full-time faculty members have more than 20 years of experience in diagnosing and managing patients with lymphoma. More importantly, the disease management team that involves these and other specialists — including medical oncologists, hematopathologists, and diagnostic radiologists — meets each week to discuss difficult cases. Our group also discusses all newly referred patients on a weekly basis to ensure a uniform management approach.

This consistency and breadth of shared knowledge helps to ensure that patients receive the best treatment options possible in the world today. Our team has extensive experience in managing even the rarest types of lymphomas, such as Burkitt lymphoma, Waldenstrom macroglobulinemia, and different types of T cell lymphoma.

Our Lymphoma Service is tight-knit, and we continue to add to it: We were pleased to welcome one of our star fellows, medical oncologist and hematologist Anita Kumar, as a full-time faculty member in August 2014.

OUR STREAMLINED EFFICIENCY

The average time from when patients first call us to when we see them in our clinic is five days. We achieve this through the use of a centralized referral process (call 800.525.2225 from Monday through Friday, 8:30 AM to 5:30 PM ET). Many of our referring physicians also continue to contact faculty members directly to discuss patients before deciding to make a referral or having a patient make an appointment.

> "Our team has extensive experience in managing even the rarest types of lymphomas, such as Burkitt lymphoma, Waldenstrom macroglobulinemia, and different types of T cell lymphoma."
>
> — ANAS YOUNES , MD

OUR INNOVATIVE TREATMENTS

While we continue to provide state-of-the-art care to all of our patients, our numerous clinical trials also offer innovative treatment options, from the use of small molecule inhibitors to genetically engineered T cells for relapsed lymphoma and strategies aimed at stimulating the patient's own immune cells to fight lymphoma. Our continuously updated clinical trials listings reveal the breadth and scope of our portfolio.

OUR CUTTING-EDGE FACILITIES

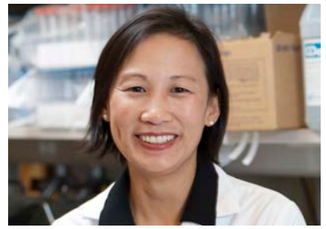
Recently opened at our 64th Street Outpatient Center, our new "clinic of the future" provides an ideal environment to enhance the patient experience and promote education and interaction with our team while ensuring the utmost comfort for family members and caregivers.

OUR PERSONALIZED CARE

Many treatment options are available to people with lymphomas today. With recent advances in our understanding of the varying biology, proteomic biomarkers, and genetics of each person's lymphoma, our approach to each patient is becoming increasingly individualized. Treatment options can now be tailored to provide patients with the most promising treatments based on their specific tumor type.

Katharine C. Hsu, MD, PhD

ASSOCIATE ATTENDING, ADULT BMT SERVICE



KATHARINE HSU considers blood and marrow transplantation (BMT) to be the forefather of immunotherapy, which has become increasingly pivotal in emerging cancer therapies. Dr. Hsu, who joined the BMT team at Memorial Sloan Kettering after completing a hematology oncology fellowship here in 1997, harbors a lifelong interest in immunology and BMT that makes her a natural fit for her role.

Calling herself a physician first "but with a healthy dose of scientific inquiry," Dr. Hsu's laboratory work focuses on the role of natural killer (NK) cells, which are integral to innate immunity and can recognize and kill virally infected cells and tumor cells. Her research has investigated how NK cells control leukemia relapse in BMT patients, showing that specific combinations of immune molecules known as human leukocyte antigens (HLA) and killer Ig-like receptors (KIR) — which are found on the surface of NK cells — can predict improved outcomes in transplant patients.

Dr. Hsu and her colleagues are also exploring the role of NK cells in controlling other malignancies, such as the pediatric tumor neuroblastoma. Her research has led to a new treatment protocol combining the use of monoclonal antibodies with NK cells for high-risk neuroblastoma patients.

Here, Dr. Hsu discusses her path toward oncology, along with the impact of her research on BMT donor selection and her future aspirations in the field.

What factors guided your decision to go into medicine?

I have always been interested in immunology, and in high school, I started working in a laboratory at City of Hope Cancer Center in Southern California. Even then, we were using cutting-edge techniques at the time to determine some of the molecular markers that characterized pediatric leukemias. The granddaddy of all immunotherapies is in some ways BMT, because it's not simply a replacement of sick marrow with healthy marrow — it's a therapy where the replacement marrow fights the sick marrow. There is still lot about BMT we don't fully understand, but it is clear that one of the cells that fights leukemia is the natural killer cell.

How has your research on natural killer cells impacted patient outcomes so far?

We have developed a new algorithm for selecting our donors. Transplant has now grown to encompass a large variety of different stem cell donors – related donors, siblings, unrelated donors, and umbilical cord blood donors. Ultimately we want to cure the patient of their disease, and the choice of donor may influence the likelihood of cure. There should be discrete algorithms for deciding which donor gives a patient the best chance at eradicating or controlling their disease. A large part of my clinical research has focused on developing those donor algorithms based on KIR and HLA. We are extending these studies to a large multicenter study, with the express purpose of helping transplant centers select donors for their leukemia patients.

Which aspects of BMT still need more of a research emphasis?

Several aspects of transplant need improvement, in particular the significant risk of leukemia relapse following transplant. There is nothing more heartbreaking for the physician and patient than for a patient to undergo a transplant, only to have his or her disease return. We need to identify the factors, such as tumor burden and genetics, that influence the likelihood of relapse following transplant and determine how we can we optimize these factors.

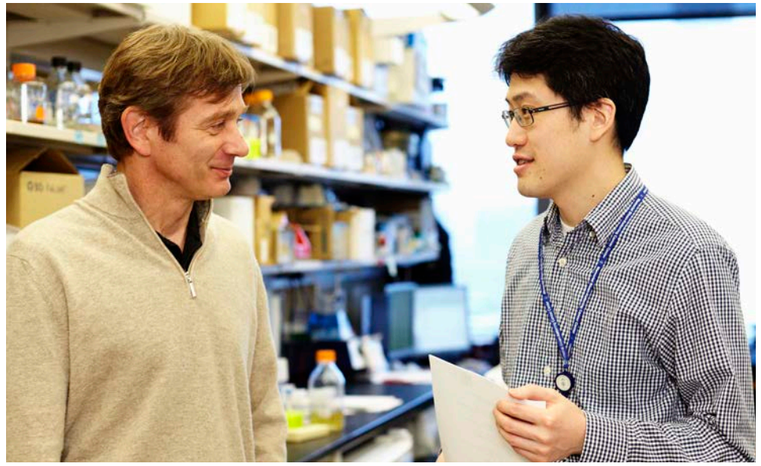
Secondly, we need to reduce transplant complications, such as infections and graft vs. host disease, inherent to transplant and immunosuppression. These major complications contribute to an unacceptable risk of transplant-related mortality. NK cells are shown to reduce the risk of both, so there is great promise for NK cell research to hit all of these known post-transplant complications.

What is your dream project in terms of BMT research or outcomes?

If we can understand what turns on an NK cell, and if we can interfere with the signals that turn off an NK cell, wouldn't it be wonderful if we could control NK cells so leukemia patients wouldn't need a transplant at all? NK cells can be extremely potent, but certain signals can turn them off. We are currently working with an antibody aimed at interfering with the off-signals. We'll see how successful it is, but I think we have more work to do.

Bacteria May Hold the Key to Preventing Dangerous Side Effect of Transplants

Research suggests that the presence of a type of bacteria called Blautia, which occurs naturally in the body, may prevent graft-versus-host disease, a potentially fatal side effect of bone marrow and stem cell transplants.



MARCEL VAN DEN BRINK (LEFT) AND ROBERT JENQ

IN JANUARY 2013, a major milestone was reached when the world's one millionth blood stem cell transplant was performed. Beginning in the 1970s, bone marrow and blood stem cell transplants — also known as BMTs — have offered the chance of a cure for many people with leukemias, lymphomas, and other blood disorders.

But since patients first began receiving this treatment, a major complication of allogeneic transplants, in which patients receive stem cells or bone marrow from a donor, has been graft-versus-host disease (GVHD).

GVHD occurs when newly transplanted immune cells from the donor recognize the recipient's tissue as foreign and attack it. The condition can be temporary or chronic and can result in damage to the liver, lungs, digestive tract, or other organs. In some cases it is fatal.

Memorial Sloan Kettering physician-scientist Robert Jenq is one of many investigators studying the disease. His particular research is focused on the role of bacteria and how certain bacterial strains that are naturally found in the body may protect against GVHD. At the BMT Tandem Meeting in February 2014 held in Grapevine, Texas, he presented a study that was selected as one of the six best abstracts of the meeting.

We spoke to Dr. Jenq about his research and how it might someday benefit patients.

STUDYING THE MICROBIOTA

"Since the 1970s, we've known that the bacteria that live in the gastrointestinal tract — the microbiota — have an impact on the risk for GVHD," he says. "We tried to apply some of the early discoveries we made in mouse models to patients, but in the end they didn't work."

Fast-forward to the advent of computational biology. Advances in computing power over the past decade have made it possible to make sense of vast amounts of genetic data coming from populations of bacteria living in the human body. "New genetic sequencing technologies have helped us to characterize all the bacteria that live in the gastrointestinal tract in great detail," Dr. Jenq explains. "This approach is something that wasn't possible even a few years ago."

Aiding in the development of new research is the Human Microbiome Project, an ongoing, multi-institutional initiative funded by the National Institutes of Health that aims to characterize and provide detailed insight into the complexity of all of the microorganisms that live inside us.

Previous studies from Dr. Jenq and his colleagues, including Hematologic Oncology Division Head Marcel van den Brink, began looking at how the balance of intestinal bacteria can affect GVHD. One of their areas of focus has been how antibiotics given to patients during the course of treatment to either relieve or prevent infections may have a negative effect on the so-called good or healthy bacteria that live in the body.

> "New genetic sequencing technologies have helped us to characterize all the bacteria that live in the gastrointestinal tract in great detail. This approach is something that wasn't possible even a few years ago."
>
> — ROBERT JENQ, MD

A BACTERIUM CALLED BLAUTIA

The latest study, done in collaboration with Dr. van den Brink and infectious disease specialists Eric Pamer and Ying Taur, focused on a genus of bacteria called Blautia. "Using sequencing technologies to study the bacterial makeup of the gastrointestinal tracts of patients undergoing BMTs, we found that if patients had even a smidgen of Blautia left — just 0.1 percent of the total makeup of bacteria in their GI tract was Blautia — they had an almost negligible risk of GVHD," Dr. Jenq says.

The investigators took their findings back to mouse models and found that giving Blautia to mice that had lost it could protect them against GVHD.

"Blautia is a harmless type of bacteria that every patient comes in with, but a lot of them lose it during the course of transplantation," he adds. "It seems to be sensitive to the antibiotics that patients are given during the course of treatment, and it also declines in patients who aren't eating, a common situation in BMT patients."

Currently, GVHD is treated with powerful immune suppressants. "It's necessary because GVHD can be fatal," Dr. Jenq says, "but these drugs increase the risk that patients will develop infections and also that their cancer may come back. Our findings about Blautia open up new avenues for preventing GVHD."

NEW APPROACHES TO PREVENTING GVHD

One solution may be giving patients only types of antibiotics that do not affect Blautia. In addition, encouraging patients to eat during their transplants rather than providing them with their nutrition intravenously may help to keep their Blautia alive. "When you supply nutrients by IV, you're feeding the patients but you're not feeding their bacteria," Dr. Jenq notes. "That may be important."

Another approach could be finding a way to give patients beneficial bacteria such as Blautia after their transplants. (This is the basis of the idea behind the food supplements known as probiotics.)

Some studies have suggested that the role of Blautia in the gastrointestinal tract is to produce compounds called short-chain fatty acids, which researchers believe help to suppress inflammation. "If this proves to be true, we may be able to bypass the bacteria completely and just give as a treatment the compounds the bacteria are producing that mediate the beneficial effects," he says. "We call this strategy 'postbiotics.'"

All of these possibilities need to be evaluated further before any clinical studies can begin in patients. "Testing all of these strategies in mice will shape whatever trials we do in the future," Dr. Jenq concludes.

THIS RESEARCH WAS SUPPORTED BY THE NATIONAL INSTITUTES OF HEALTH UNDER GRANT NUMBER R01 AI100288 AND BY THE LUCILE CASTORI CENTER FOR MICROBES, INFLAMMATION, AND CANCER AT MEMORIAL SLOAN KETTERING.

CLINICAL TRIAL

Can Cells Be Turned from Cancerous to Normal?

An experimental drug for blood cancers with certain genetic mutations is showing promise in early-stage trials.

HISTORICALLY, CANCER TREATMENT has aimed to eliminate cancer cells, whether through traditional methods such as surgery, chemotherapy, and radiation or newer treatments such as targeted therapies and immunotherapies.

But a new approach is gaining attention that turns the seek-and-destroy tactic into more of a search-and-rescue one, by transforming cancer cells into normal cells instead of killing them. So far, it's showing early promise in treating certain kinds of leukemia and other blood cancers.

"Leukemia occurs when immature cells are able to accumulate in the blood," says Memorial Sloan Kettering hematologist Eytan Stein. "These cells, which form in the bone marrow, contain mutations that prevent them from differentiating into specialized blood cell types. If we can find drugs to block the enzymes that prevent the cells from maturing, we may have a way to cure the leukemia."

Dr. Stein is leading a study evaluating one of the first drugs to take advantage of this approach. He presented early findings at the American Society of Hematology (ASH) annual meeting in San Francisco in December 2014. The study was also featured in The Wall Street Journal.

BLOCKING MUTANT ENZYMES

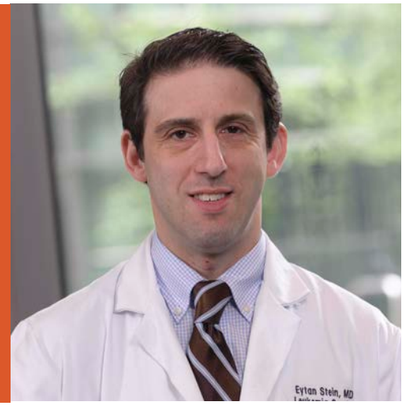
The drug, called AG-221, works by blocking enzymes made from a mutant form of the gene IDH2. The normal IDH2 protein is found in every cell of the body and plays a role in the biochemical process by which the cell makes energy.

"Certain IDH2 mutations induce cells to take on a life of their own," Dr. Stein explains. "They cause them to produce enzymes called oncometabolites, which prevent normal blood stem cells in the bone marrow from differentiating into immune cells called neutrophils."

The current study included patients with a variety of blood cancers caused by IDH2 mutations, primarily acute myeloid leukemia and myelodysplastic syndrome. Of the 45 patients who were on the drug long enough to be evaluated, 25 had a response, and five responded well enough to be able to undergo a bone marrow transplant, the current standard of care.

Analysis showed the level of oncometabolites was greatly reduced in patients taking AG-221, an indication that the drug was reaching its intended target.

> "If we can find drugs to block the enzymes that prevent the cells from maturing, we may have a way to cure the leukemia."
>
> — EYTAN STEIN, MD



TRANSFORMING TREATMENT

"With the exception of only one other drug called ATRA for the treatment of acute promyelocytic leukemia, this is not the usual way to treat cancer," Dr. Stein notes. "This approach is truly transformative — both because it changes the way we look at cancer and because it literally transforms cancer cells."

AG-221 is taken as a pill at home, "and we know it improves patients' quality of life if they don't have to go into the clinic and receive chemotherapy," Dr. Stein says.

"In addition, these cancers often occur in older people who frequently can't get traditional chemotherapy because of other health problems."

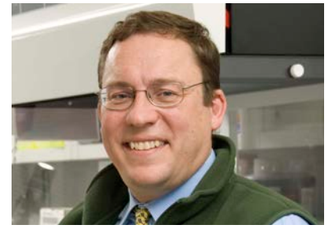
The investigators stress that this drug is still in the very early stages of testing, but they have already expanded the phase I trial to include more patients based on the promising results so far.

In addition to Dr. Stein's study, MSK had two other studies featured in the press program at the ASH meeting, the most from any single institution. Both were related to the treatment of Hodgkin lymphoma. One study found that giving patients a targeted antibody drug as maintenance therapy after bone marrow or stem cell transplant improved survival; the other found that an immunotherapy drug improved outcomes in patients who had failed to respond to standard treatment.

INTERVIEW

Renier J. Brentjens, MD, PhD

ASSOCIATE ATTENDING, LEUKEMIA SERVICE
DIRECTOR, CELLULAR THERAPEUTICS



MEET RENIER J. BRENTJENS, a physician-scientist whose laboratory research has pioneered novel immunotherapies for certain leukemias. A member of Memorial Sloan Kettering since 1998, when he arrived as a medical oncology fellow, Dr. Brentjens' seminal research with colleagues alters T cells from patients' own immune systems to seek out and attack their cancer cells.

Dr. Brentjens considers it a "unique opportunity" to perform lab research that's directly relevant to the patients he treats. He has led small clinical trials testing an immunotherapy approach called adoptive cell transfer (ACT) that have produced remarkable responses in patients with advanced acute lymphoblastic leukemia (ALL) with few if any treatment options remaining.

The ACT approach genetically engineers T cells to produce special surface receptors known as chimeric antigen receptors, or CARs. CAR proteins enable T cells to recognize antigens on tumor cells, and the engineered CAR T cells are then greatly expanded in the laboratory before being infused into the patient, further multiplying, and killing cancer cells that bear the surface antigen.

Here, Dr. Brentjens discusses how he blends patient care and research at MSK to raise the bar on leukemia outcomes.

How has your lab research evolved during your tenure at Memorial Sloan Kettering?

As a medical oncology fellow still in training, I started developing a gene to encode a new type of receptor I could put in patients' own immune cells to make the cells recognize and kill cancer cells. First I tried getting immune cells to kill cancer cells in a petri dish, and over the years it evolved to determining if the approach worked in mice. Ultimately, after a lot of further development, we were able to test whether this approach actually works with patients whose cancers were no longer responding to chemotherapy.

Which aspects of leukemia have seen the most research in recent years?

Significant advances have been made in the types of treatments available for chronic lymphocytic leukemia, a slow-growing type, as well as several new and exciting drugs that appear to work in patients who have had multiple chemotherapies in the past. These add to our ACT approach to treat patients with ALL, which is a much faster-growing cancer.

While we at MSK were the pioneers of those ACT treatments, several other institutions have developed similar programs, including the National Cancer Institute, University of Pennsylvania, and Fred Hutchinson Cancer Institute in Seattle. What's exciting is that their reported results are very similar to the results we've published. We've been doing this for 17 years, but now there's a great effort to expand this to multi-center trials, with the primary goal of making this approach a standard of care for this disease. We're confident that will take place.

How has your research impacted patient outcomes so far?

Many novel treatments and therapies for leukemia initially started as clinical trials here at Memorial Sloan Kettering. In contrast to community doctors and oncologists, we not only have access to the newest and most exciting therapies, but leukemia treatment practices developed here are the ones most likely to dictate the new standard of care.

With our cell-based ACT therapy, we've seen the greatest success in relapsed B-cell ALL, a diagnosis that in adults is almost universally fatal. Our treatment has been able to take patients who otherwise have no options and induce remission in about 90% of them, serving as a beacon of hope. The results we've seen in clinical trials offer proof of principle that we're on the right track. But we're continuing to develop this technology so patients in remission remain in remission, and to investigate whether we can use this therapy up front rather than wait for a patient to relapse.

What energizes you about your research?

I think many young investigators go into the field of oncology with a very sincere hope of having an impact directly on the lives of patients. To that extent, I'm an extremely fortunate scientist because I have actually been able, through my own work and that of my colleagues, to take such idealistic hopes and make them a reality. Really, what I do is not a job, it's a wonderful adventure.

How is leukemia research at MSK set apart from other institutions both nationally and internationally?

In our Leukemia Service, the research is very multifaceted. On one hand, we conduct first-rate laboratory research that has an additional translational component that's very difficult to achieve, taking what seems to be successful in mice and applying it to humans. We're extremely unique because very few centers are able to do that.

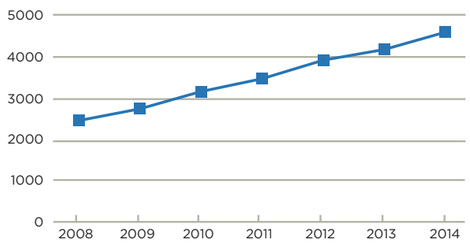
We also have a very strong tradition in clinical trial development and in testing new medications coming from the industry. So if you're a patient with leukemia coming to MSK, we offer not only the best care for your given leukemia, but also give you access to state-of-the-art treatments, some of which are very promising while still under development.

What do you hope to accomplish next?

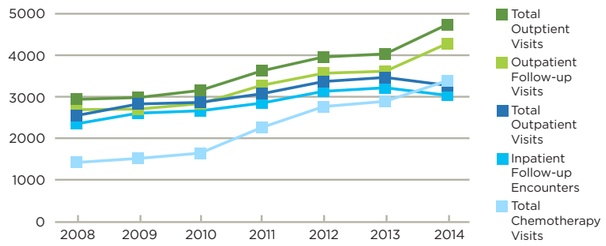
There's still a lot of work to be done on our ACT approach. To that extent, we've developed even more potent gene therapy approaches that we're very eager to move into the clinical setting, hoping to improve outcomes for patients not only with acute leukemias, but also slower-growing chronic lymphocytic leukemias and non-Hodgkin lymphomas. It's exciting that the approach we've developed seems to work, and even more exciting that there's room for improvement and we've already identified ways this can be achieved.

Division of Hematologic Oncology Metrics

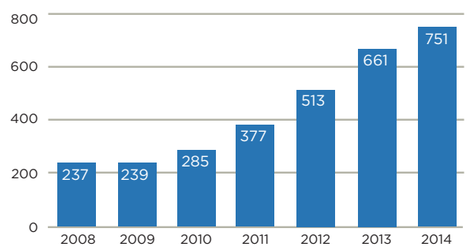
Hematologic Oncology New Visits



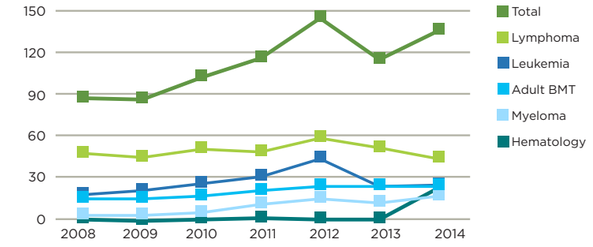
Hematologic Oncology Visits



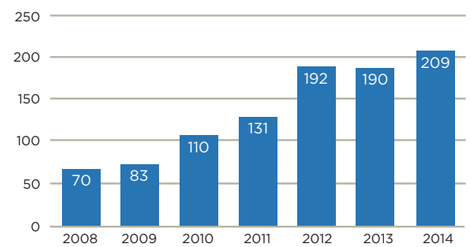
Clinical Trial Accruals — Therapeutic



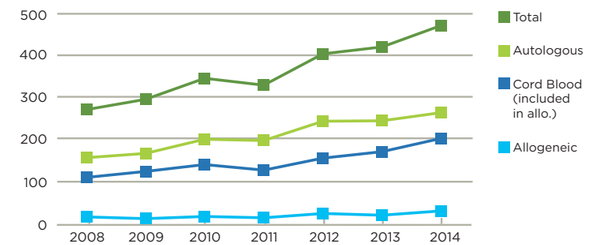
Number of Open Therapeutic Clinical Trials



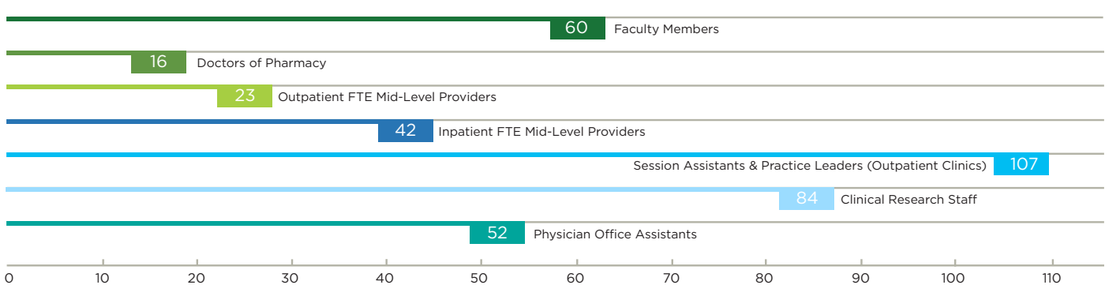
Peer Reviewed Publications



Adult Bone Marrow Transplant Facts and Figures



Staff 2014



MSK West Harrison

MEMORIAL SLOAN KETTERING'S new West Harrison outpatient facility opened on October 6, 2014. The 114,000-square-foot facility is home to a staff of 140 cancer surgeons, oncologists, radiologists, and other healthcare professionals. The modern, intuitive space is designed to maximize patients' comfort and includes amenities like valet parking, Wi-Fi, a grab-and-go fresh food counter, and a peaceful outdoor garden. From screening and surveillance to treatment and survivorship, MSK's newest suburban outpatient treatment center brings our expertise to patients in New York's Westchester County and surrounding communities.

"If we can decrease the burden of travel, patients will spend less time commuting and more time in the comfort of their own homes, which is important in the healing process," explains Richard R. Barakat, Deputy Physician-in-Chief for MSK's Regional Care Network and Cancer Alliance.

Other offerings for patients include genetic counseling, nutrition consultations, and social-work support. And a wide range of clinical trials — including early-stage studies of novel targeted anticancer drugs, specialized on-site staff, and dedicated lab space — allow patients to receive new treatments and schedule their follow-up appointments at MSK West Harrison.

"Clinical trials are critical for translating scientific discoveries into new treatments that improve patient care," says Ephraim Casper, Medical Director of MSK's Regional Care Network.

HEMATOLOGIC ONCOLOGY FACULTY CURRENTLY PRACTICING IN THE REGIONAL NETWORK

Philip Caron*	MSK SLEEPY HOLLOW
Pamela Drullinsky*	MSK ROCKVILLE CENTRE
Audrey Hamilton*	MSK BASKING RIDGE
Paul Hamlin	MSK BASKING RIDGE
Hani Hassoun	MSK WEST HARRISON
Sham Mailankody†	MSK COMMACK
Michael Mauro	MSK WEST HARRISON
Matthew Matasar	MSK COMMACK
Andrew Zelenetz	MSK WEST HARRISON

*PRIMARY LOCATION † STARTING 9/2015

MSK'S NEWEST SUBURBAN OUTPATIENT TREATMENT CENTER IN WEST HARRISON, NY.

"For many, clinical trials offer the most promising treatment options available. The opportunity to participate in our trials is one of the special benefits of treatment at MSK, and patients who live in Westchester, the Hudson Valley, and [southwestern] Connecticut will have access to the latest clinical trials close to home."

MANY OF OUR DOCTORS LIVE IN THE COMMUNITY

"When we began thinking about clinicians who might want to work in West Harrison, rather than thinking only about hiring new people who may not be familiar with the MSK culture, we came up with a new model," Dr. Barakat says. "We have physicians and surgeons who have been at MSK — in some cases for many years — and even chiefs of services, who live in the community and who will be working at West Harrison. This allows us to truly infuse the MSK multidisciplinary culture into this new facility."

Physicians and surgeons who practice at MSK's Manhattan locations but reside in the Hudson Valley are extending their practices into their own community. "MSK doctors, nurses, and support staff will be seeing patients not only professionally but also as part of their daily lives," Dr. Barakat observes. "They'll be running into these same people in their churches, their temples, at the grocery, at social events. We are already full participants in the life of the community and are here to help."

MSK BASKING RIDGE
136 Mountain View Boulevard
Basking Ridge, NJ 07920

MSK COMMACK
650 Commack Road
Commack NY 11725

MSK HAUPPAUGE
800 Veterans Memorial Highway, 2nd Fl
Hauppauge, NY 11788

MSK WEST HARRISON
500 Westchester Avenue
Harrison, NY 106043

MEMORIAL SLOAN KETTERING CANCER CENTER
1275 York Avenue
New York, NY 10065

MSK ROCKVILLE CENTRE
1000 North Village Avenue
Rockville Centre, NY 11570

MSK SLEEPY HOLLOW
777 North Broadway
Sleepy Hollow, NY 10591

FUTURE SITE
MSK MONMOUTH

The Oncology Clinic of the Future Is a Reality at Memorial Sloan Kettering

PAUL A. HAMLIN, MD

With innovative advances in technology and "smart rooms" responsive to individual patients, our Clinic of the Future is a thing of the present.

IMAGINE what a futuristic oncology clinic might be like.

Before your treatment, your mobile device reminds you of your appointment time and location at Memorial Sloan Kettering and notifies you that appointments are running on schedule.

When you arrive, the "smart building" automatically checks you in, alerting the phlebotomy unit and your treatment care team that you've arrived. A greeter escorts you to the phlebotomy unit and then into the consultation room, where you settle into a comfortable chair. The reassuring face of your sister appears on a videoconferencing screen, virtually placing her in the room with you.

The technologically integrated room announces each person on your team by name and job function. Your doctor explains your treatment plan as you review PET scan images together on a monitor and discuss your next visit. The team answers all your treatment questions, and the nurse sends you video versions of the educational material and clinical trial synopsis to review at home.

A REAL-TIME LABORATORY IN INNOVATION

The MSK Clinic of the Future at our 64th Street Outpatient Center is already implementing these types of cutting-edge practices for patient care and clinical research in people with lymphomas and multiple myelomas.

The space, opened in June 2014, was designed in collaboration with patients, doctors, nurses, and top architects and design teams and aims to fashion an experience that will serve as a proving ground for the future.

Waiting areas feature rotating art exhibits (including pieces by patients and staff) and provide charging stations and work areas for patients and families. Our consultation rooms are an intimate space that seamlessly transforms from examination to consultation mode via subtle lighting shifts and specially designed chairs.

Behind the scenes, real-time location services allow patients to freely move about the clinic. Patients and staff wear unobtrusive radio-frequency ID cards that enable us to automatically check people in to phlebotomy and dynamically assign consultation rooms, resulting in decreased wait times, increased transparency about delays, and timely updates — improving efficiency and work flow.

NEW INTEGRATED CHEMOTHERAPY INFUSION SUITE UTILIZING REAL TIME LOCATION SERVICES

CHEMOTHERAPY INFUSION ROOM WITH CHAIRSIDE EDUCATION/MEDIA PORTAL

SMART-ROOM TECHNOLOGY

By laying the groundwork for "smart rooms" responsive to each patient, we are preparing to introduce educational content and clinical research materials using in-room video portals that reflect an individual's specific needs.

Through wireless technology, patients and physicians can review laboratory or radiology results eye to eye. Physicians can share information on their screens to examine trends in laboratory findings, view radiographic images, and coordinate care.

Simultaneously, we're building a video library of educational and clinical research materials to convey essential information about cancer care and treatment — all of which can be seamlessly shared via email and patient portals.

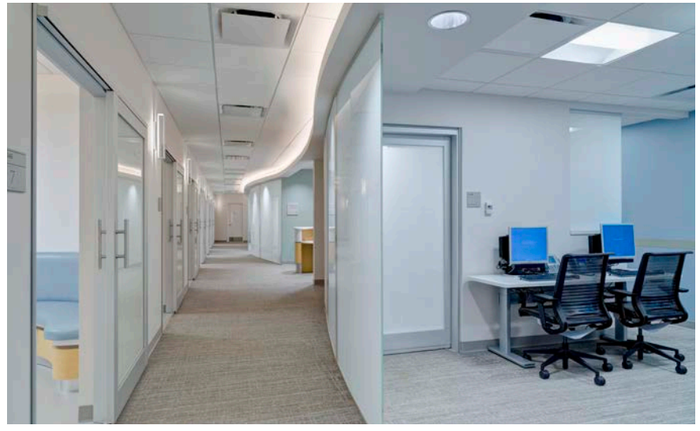
The multimedia content will initially include nursing materials on managing symptoms, wellness content, nutrition advice, and clinical-trial briefs that present concepts in an understandable manner.

THE "WHY" OF THE CLINIC OF THE FUTURE

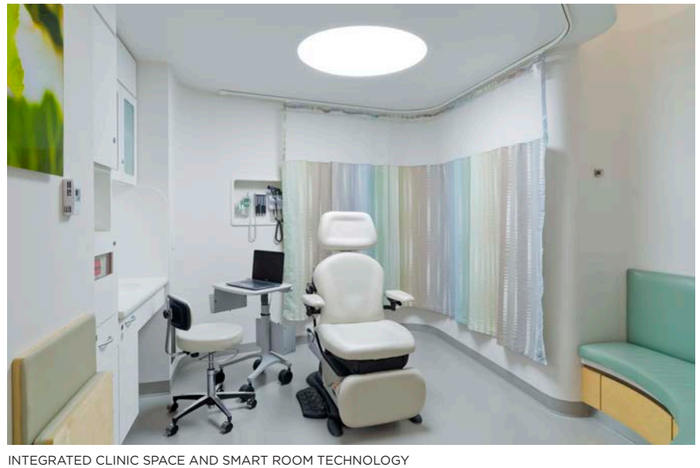
At the heart of all of these efforts is our relentless drive to offer the very best cancer care in the world, centered on the specific needs of each patient.

By boosting our ability to work as a team in embracing each patient and shaping individual treatment plans, the clinic enables us to provide the latest in cutting-edge approaches to diagnosis, treatment, and ultimately, the conquering of cancer.

NEWLY DESIGNED PATIENT CENTRIC WAITING AREA



CLINIC SPACE AND TEAM WORKROOMS



INTEGRATED CLINIC SPACE AND SMART ROOM TECHNOLOGY

American Society of Hematology (ASH) Meeting 2014

SAN FRANCISCO, CA

AT THE 56TH ANNUAL MEETING of the American Society of Hematology in San Francisco, California, our faculty was well represented with over 150 abstracts, 55 of which were selected for oral presentation.

On December 6, 2014, the Memorial Hospital Alumni Society hosted their seventh annual alumni reception at the annual ASH meeting at the Marriott Marquis Hotel. The reception was well attended by MSK alumni, current faculty, fellows, and colleagues from other institutions as well as invited guests of the MSK Division of Hematologic Oncology.

Before the ASH Meeting, co-chairs Dr. Marcel van den Brink (MSKCC) and Dr. Edmund Waller (Winship Cancer Institute, Emory University) and co-hosts Dr. Lloyd Damon (UCSF) and Dr. David Miklos (Stanford University) led the Third Annual BMT Winter Workshop at the University of California, San Francisco (UCSF) Mission Bay campus. The workshop was attended by 250 physicians and scientists and consisted of short presentations regarding unpublished recent research on Hematopoietic Stem Cell Transplantation.

LEFT TO RIGHT: RENIER BRENTJENS, CRAIG SAUTER, MARCEL VAN DEN BRINK, EYTAN STEIN, AND MARTIN TALLMAN

STEVEN HORWITZ, ALISON MOSKOWITZ, AND MATTHEW LUNNING

MIGUEL PERALES AND KEITH STEWART (MAYO CLINIC)

BMT Tandem Meeting 2014

GRAPEVINE, TX

MSK'S ACHIEVEMENTS in blood and marrow stem cell transplantation took center stage at the 2014 BMT Tandem Meeting, a joint conference of the American Society of Blood and Marrow Transplantation (ASBMT) and the Center for International Blood and Marrow Transplant Research (CIBMTR.)

Sergio Giralt served as ASBMT President during 2014 and worked collaboratively with members to further the society's goals of promoting all aspects of blood and marrow transplantation, including cellular therapy research, education, scholarly publication, and clinical standards. During the annual meeting in February 2014, which took place in Grapevine, Texas, Dr. Giralt hosted a Texan-style evening organized by MSKCC.

ESSIE PAPADPOPULOS, ALAN HANASH, AND ROB JENQ

DAVID CHUNG, MEIGHAN PALAZZO, DUNCAN PURTILL, AND KATIE KILROY

HIGHLIGHTS

- SERGIO GIRALT, Chief Attending of the Adult BMT Service, assumed his role as ASBMT President for 2014-2015
- ALAN HANASH received a $240,000 award from the Amy Strelzer Manasevit Research Program
- MSKCC physician-scientists ROBERT JENQ and YUSUKE SHONO presented two of the six "best abstracts" highlighted at the meeting, which were chosen from a total of 528 abstracts submitted from 30 countries.
  - ROBERT JENQ: "Identification of Intestinal Commensal Bacteria Protective Against GVHD in Mice and Humans"
  - YUSUKE SHONO: "ATG16L1 Prevents Lethal T-Cell Alloreactivity Mediated By Dendritic Cells"
- RICHARD O'REILLY, Chair of the Department of Pediatrics and Chief of the Pediatric Bone Marrow Transplant Service, delivered the E. Donnall Thomas Lecture, which recognizes an eminent physician or scientist who has contributed meritoriously to the advancement of knowledge in blood and marrow transplantation. Dr. O'Reilly founded the then-combined adult and pediatric Bone Marrow Transplant Service at Memorial Sloan Kettering more than 30 years ago as one of the original transplant centers in the United States. Since that time, the program has pioneered many significant advances in the field, including the first transplant of bone marrow from an unrelated donor to a patient in 1973. In his lecture, Dr. O'Reilly reviewed the history of T-cell-depleted marrow transplantation.

Steven M. Horwitz, MD

ASSOCIATE ATTENDING, LYMPHOMA SERVICE

STEVEN M. HORWITZ was interested in finding an institution large enough to allow him to narrow his clinical research to rare types of lymphoma. Memorial Sloan Kettering proved to be that place. Dr. Horwitz, who joined the faculty in 2001, spends his time developing new therapies for T-cell lymphoma and cutaneous (skin) lymphomas.

Lymphoma is a disease encompassing nearly five dozen related types of cancer of immune cells; diagnosis and treatment relies on a patient's specific subtype of Hodgkin or non-Hodgkin lymphoma. Patients with T-cell lymphoma comprise about 15% of those with the non-Hodgkin variety, leaving Dr. Horwitz in rare company as he tackles this unusual – and at times unusually challenging – form of the disease.

Here, Dr. Horwitz details the evolution of his clinical research and the need for networking among physician-scientists working with rare diseases.

Why did you decide to concentrate your research on new therapies for less-common types of lymphoma?

In 1997, when I was starting my fellowship, rituximab was just approved for B-cell lymphoma and there was a tremendous amount of momentum directed at B-cell lymphomas. It seemed that the T-cell lymphomas were being left behind. Also, I was seeing a lot of patients with cutaneous T-cell lymphomas, so I became very involved with taking care them. There are many aspects of managing these patients that are different from other lymphomas and cancers. It was an area where I felt I could make a contribution. Not many others were working on these diseases, so there was a need and an opportunity.

How has your research evolved during your tenure at MSK?

When we first started, it wasn't really clear how to best approach these diseases. First we were looking at clinical data sets and establishing where standard therapies were working and not working. We already knew a lot of treatments were borrowed from other lymphomas, so we looked for new drugs with specific activity in T-cell lymphomas. Since 2009 we've had 4 FDA-approved, so we've had some success. Many of our studies now look at combinations of drugs – which I think will be necessary if we want to significantly change outcomes.

Which aspects of lymphoma still need more of a research thrust?

The main problem in T-cell lymphoma is that we just don't have a treatment that helps the majority of patients. We have treatments that help a minority, but we really need more effective therapy overall. Some patients are cured with some of our combination chemotherapy strategies, even if chemotherapy is imprecise, so we don't want to veer away from those too quickly. Because if you're cured of lymphoma, even through imprecise means, you're still cured of lymphoma. We're now doing a better job of identifying who does best with standard therapy, but if we could identify those least likely to benefit, we could individualize their therapy and take them down a different path early on and apply different strategies.

How has your research impacted patient outcomes so far?

We have identified a lot of interesting new therapies and we have a lot of patients who've benefited individually. But the median survival for T-cell lymphoma still hasn't improved, and we want excellent therapy for everyone. With Hodgkin's lymphoma, for example, 80% to 90% of patients are cured with standard therapies. But not that many treatments for T-cell lymphoma yield even a 50% response, and the durations of response are often short. We are trying to find new therapies to get more people into remission and keep them in remission longer. Compared to when I started, many more people are doing better, but it's a process and we still have a long way to go.

How is lymphoma research at MSK set apart from other institutions both nationally and internationally?

Collaboration is a must when you're working with rare diseases, and we work with doctors nationally and internationally and make a significant contribution to these joint efforts. But what does MSK have that others don't? Our strengths are very broad. We have excellent investigators and researchers who bring forth fantastic and creative ideas. We also have a large patient population that's tremendously motivated and wants to participate in research not only to get themselves better, but contribute to the field. Compared to other centers, we have strengths in most areas, whereas a lot of those we work with may be strong in only one or two things.

What challenges still confront you in your research?

As much as we are learning individual tumors, our treatments are still pretty empiric. While we have tools to better understand these diseases, in T-cell lymphoma we don't have many animal models to gain insight into how treatments will behave until we get them to people. The rarity of the disease makes this more difficult and progress feels too slow, which is one of the reasons we focus on collaborating with other centers.

What's your ultimate goal in terms of research and outcomes?

That we will get to a point where we look at a person's diagnosis, understand their tumor, and use treatment combinations we are confident will work for them. It will likely be a long process to get to that point, but I believe we will get there and selfishly I hope our research at MSK will be an important part of it.

C. Ola Landgren, MD, PhD

CHIEF ATTENDING, MYELOMA SERVICE

SEEKING A TRAILBLAZER in myeloma research and care, Memorial Sloan Kettering recruited C. Ola Landgren in May 2014 from his previous post at the National Cancer Institute. His appointment as Chief of the Myeloma Service was fortuitous for all involved, with Dr. Landgren — a pioneer in the development of minimal residual disease (MRD) testing in myeloma — planning to "put MSK on the map both in the United States and worldwide as one of the leaders in myeloma."

In his clinical research, the Swedish-born hematologist-oncologist also studies the mechanism and markers of the progression of so-called "smoldering myeloma" to symptomatic multiple myeloma. His clinical trials in MRD assays implement new cell-based, molecular-based, and imaging-based strategies he has developed with colleagues at MSK, nationally and internationally.

In this interview, Dr. Landgren details what drew him to his new post at MSK, how myeloma outcomes are improving, and his five-year goals for patient care.

How does your work with patients drive your research?

One of the really important aspects for me as a leader of the program is not to lose contact with what's going on in clinic. It's actually a privilege as a physician-scientist to take in a 360-degree view and see results from work I've developed with the team. Very few jobs offer the opportunity to go from basic science to improving outcomes, and that's where a lot of my inspiration for new ideas comes from. Most specifically, I'm very interested in why, under the microscope, patients may appear to have the same disease but end up having such different outcomes. We also know that in any single patient, there's more than one subtype of multiple myeloma going on at the same time.

When we discover these pathways, we're trying to evaluate the drugs that would make the most sense and use them.

What enthuses you about your research?

I'm very excited about opportunities to debulk myeloma with drugs we already have to the point where we almost can't detect any disease. It's thrilling that we've reached this point so soon — I've been working on this for 10 years, but in the past two to three years, advances have been made every six months that exceed what used to take five years. If we can pin down the biology of those residual cells and find the marriage between them and the right drugs, could we develop a curative strategy? That's what we're working toward. We've even moved into asymptomatic patients with high-risk smoldering myeloma. My five years of work on this topic at the NCI showed if we treat patients with early disease, 100% reach a complete response. So I'm very excited we've delivered therapies for early disease and have the tools to monitor residual disease that push the envelope.

What obstacles still stand in the way of better myeloma outcomes?

We have the tools to look the enemy in the eyes. We can see what these residual cells look like, but we're trying to figure out why they escape therapy, trying to characterize the disease up front. The other end of the spectrum is what people refer to as high-risk disease, where 25% of patients who all receive the same treatment will have a poorer prognosis. In the past 10 to 15 years, survival rates of myeloma patients in the U.S. has doubled or tripled. But for the one-quarter experiencing no improvement from therapy, clearly their disease is very different. Myeloma is not one disease; it's an umbrella term for many underlying biological processes that share features under a microscope that look the same. We need to try to carve out the details.

Why should myeloma patients seek care at Memorial Sloan Kettering instead of another institution or private practice?

A lot of new treatments available for myeloma are oral medications. Patients don't necessarily have to come to clinic and receive infusions; they can take a pill at home, and many of these therapies aren't so toxic. But if you're diagnosed with a disease with no established cure, like myeloma, you need to go to a top-notch institution where you have access to sophisticated tests and experts can read all details of your particular disease. The types of tests we have for MRD aren't readily available elsewhere, and patients with early, asymptomatic disease who are told they don't need treatment can actually have a very high risk of developing symptomatic disease. In trials we've developed for these patients, preliminary results indicate unprecedented patient responses as well as duration.

What do you hope to accomplish next?

My dream scenario is that within five years, we'll have evidence that we can provide a cure or long-term disease control for patients through sophisticated cell profiling, effective, non-intense therapy, and sophisticated monitoring for MRD. That, in my opinion, would set the stage for the next generation of treatment regardless of a patient's age. Historically, patients above age 70 — who comprise most myeloma patients — haven't been treated with the best drugs because they're so toxic. But now we have drugs that aren't as toxic, as well as all our tools for MRD testing. Leaving the older patients behind is absolutely wrong. I want to be able to treat patients independent of their age and really have an impact on their quality of life and survival.

The Mortimer J. Lacher Fellows Conference

LEFT TO RIGHT: PATRICK BURKE, MELODY SMITH, MORTIMER J. LACHER, MICHAEL J. KEATING, ERIC SMITH, AND AARON VINY

THE DIVISION held its annual Mortimer J. Lacher Fellows Conference on May 9, 2014. The event honors Dr. Lacher, a longtime member of MSKCC's Lymphoma Service and the Sloan Kettering Institute. Dr. Lacher joined the Lymphoma Service at Memorial Hospital in 1960 and served as a member of the Sloan-Kettering Institute from 1960 until 1990. With John R. Durant, he published a seminal report in 1965 describing the success of combining vinblastine and chlorambucil to treat Hodgkin disease. Dr. Lacher is the co-founder and current President of the Lymphoma Foundation. Every year, the Lymphoma Foundation provides funding for Medical Oncology/Hematology fellows at MSKCC and specific projects in the laboratories of MSKCC physician scientists. Dr. Lacher is now a Consultant in MSKCC's Department of Medicine.

Dr. Michael J. Keating, Professor of Medicine and Internist, Department of Leukemia, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center, delivered the Fifth Annual Mortimer J. Lacher Lecture titled, "Increasing the cure rate of chronic lymphocytic leukemia — lessons from biology."

ERIC SMITH, MD, PHD

MELODY SMITH, MD

AARON VINY, MD

The 2014 Lacher Fellows are listed below along with their abstracts:

Mythili Koneru, PhD (Mentor: Renier Brentjens, MD, PhD)
The Study of Genetically Targeted Autologous T cells with Tri-Cistronic Vectors for the Treatment of B-cell Hematologic Malignancies

Patrick Burke, MD (Mentor: Daniel Douer, MD)
Phase I/II Trial Adding an IL-JAK-STAT Pathway Inhibitor in Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia Treated with a Standard BCR-ABL Tyrosine Kinase Inhibitor to Prevent Clonal Resistance and Augment Molecular Remission Rates

Eric Smith, MD, PhD (Mentor: Renier Brentjens, MD, PhD)
Adoptive T cell therapy for multiple myeloma

Melody Smith, MD (Mentor: Marcel van den Brink, MD, PhD)
CD19-targeted donor T cells exert potent graft versus lymphoma activity and attenuated GVHD

Shunan Qi, MD (Mentor: Joachim Yahalom, MD, FACR)
Characteristics and long term treatment outcomes of 697 MALT lymphoma cases

Aaron Viny, MD (Mentor: Ross Levine, MD)
Role of the cohesin complex in oncogenic transformation of AML

Excellence in Care

RECOGNIZING MSK'S HEMATOLOGIC ONCOLOGY NURSES AND PHYSICIAN ASSISTANTS

HIGHLIGHTS

- **Jill M. Vanak, PhD, RN, BSN, MSN, ACNP-BC AOCNP** received the 2014 Heilbrunn Nurse Scholar Award, a stipend based year-long program that offers qualified graduate level registered nurses funding to engage in research focused activities at and with the support of the Rockefeller University. Jill seeks to become an independent nurse scientist researcher within the field of oncology and to develop an interdisciplinary program of research to examine outcomes of critically ill hematologic oncology patients.
- **Cheryl Gilroy, RN**, office practice nurse on the Leukemia service, served as Treasurer of the Oncology Nursing Society local Chapter, New York City.
- For the first time in 2014, the Oncology Nursing Certification Corporation offered the BMTCN™ examination, which validates an individual's specialized knowledge in blood and marrow transplantation nursing. The following nurses have successfully obtained this certification:
  - **Karen Abbondondelo**
  - **Kathy Choo**
  - **Zulay Fernandez**
  - **Kimberly Ford**
  - **Mary Giovinazzo**
  - **Pamela Grant-Navarro**
  - **Nicole Krist**
  - **Mary Montefusco**
  - **Barbara Morcerf**
  - **Joan Reyes**
  - **Joanne Taylor**
  - **Heather van den Bergh**
  - **Devin Callan**
- **Heather Hylton, MS, PA-C** provided the keynote address, "Rising to the Occasion: The Oncology Advanced Practitioner in the 21st Century" at the JADPRO Live Conference in St. Petersburg, FL, in January 2014. At this meeting, she also co-presented "The Advanced Practitioner and Social Media" with former MSK fellow, Dr. Don Dizon, and was an invited panel speaker for "Practice Matters: Bringing the Advanced Practice Horizon into Focus." Heather was also elected as a Director at Large for the Association of Physician Assistants in Oncology for 2014-2015.

M8 NURSING STAFF: BACK ROW: KATHY CHOO, INDE DUTTON, HOLLY WALLACE, PAMELA GRANT-NAVARRO, BRIDGET DIGNAN, PATRICIA ARESTA, CHELSEA MINTZ. FRONT ROW: CHRISTA PALOGLOU, ANDREA CRECCO, EMILY PANZNER, ANEILA PERSAUD

LEFT TO RIGHT: WHITNEY QUITTA PA, NANCY CRUZ SITNER NP, MARY MONTEFUSCO NP, NICOLE NIBERT PA, SARA BEKELE NP, MELISSA BASSIS NP

- **Apryl Sarabia, MS, PA-C** served as the Scholarship Chair for the Association of Physician Assistants in Oncology in 2013 and 2014.
- **Teresa Scardino, PA-C, MPAS** presented "Supportive Care for Patients with Cancer: Barriers in Achieving a Balance Between Optimizing Outcomes and Minimizing Side Effects with Chemotherapy-Induced Nausea and Vomiting" at the JADPRO Live Conference in St. Petersburg, FL, in January 2014.
- **Elaina Preston, MPH, MSHS, PA-C** and **Natalie Grome, MMSc, PA-C** presented "Bashing the Blasts: An Overview of Acute Leukemias" at MSK Physician Assistant Grand Rounds in March 2014.
- **Teresa Scardino, PA-C, MPAS** was invited faculty for the ASCO University Course "Triage: Emergency or Not?" released in March 2014.
- **Abby Staible, MMS, PA-C**, the founder of Epic Experience, a non-profit organization that seeks to engage individuals whose lives have been affected by cancer in the healing process by providing week-long experiences for cancer survivors, serves as the Medical Director of the organization and serves on the Board of Directors. **Apryl Sarabia, MS, PA-C**, **Mary Montefusco, NP** and **Joanna Zizzo, NP** served as medical volunteers in 2013 and 2014.

HEME ONC DIVISION NURSES, PHYSICIAN ASSISTANTS, & PHARMACISTS REPRESENT MSK AT 2014 BMT TANDEM MEETING

- "Safety and Efficiency of Administering Foscarnet: A Multidisciplinary Approach" **Sheila Kenny, NP** (poster presentation)
- "Amyloid Treatment Pearls: Standardizing Patient Care in Autologous Stem Cell Transplant" **Heather Hylton, MS, PA-C** and **Catherine Featherstone, NP** (poster presentation)
- "Integrating Quality Reporting into the Electronic Medical Record" **Karen Collum, RN, MSN** (podium presentation)
- "Determining the Value of Weekly Surveillance Blood Cultures as a Screening Tool for Occult Bloodstream Infection for Post Allogeneic Hematopoietic Stem Cell Transplant (HSCT)" **Gloria Coffey, NP, Lorraine Jackson, NP, Sheila Kenny, NP** and **Valkal Bhatt, PharmD** (poster presentation)

PUBLICATIONS AND PROTOCOLS

- **Featherstone C, Hylton H**. Amyloid treatment pearls: standardizing an approach to patient care. *Biol Blood Marrow Transplant* 2014:20(2): S300.
- **Wickham R, Barbour S, Scardino T.** Collaborative Practice Enhances Supportive Care in Cancer: Chemotherapy-Induced Nausea and Vomiting. *J Adv Pract Oncol* 2014;5 (Suppl 1):5-6.
- **Scardino T.** Risks for Chemotherapy-Induced Nausea and Vomiting: Capturing Relevant Data. *J Adv Pract Oncol* 2014;5 (Suppl 1):7-16.
- MSKCC Protocol Approved IRB # 15-008: "Testing a Personalize Medication Log for Patients with Lymphoma" **PI: Kim Anselmi, RN**

A Celebration of Life for Transplant Survivors

THE 19TH ANNUAL Stem Cell Transplant Survivors Celebration on October 2, 2014 brought together 250 recipients of stem cell transplants and their donors, family members and friends, doctors, nurses, and other MSK staff. The event, intended to honor the courage and continued success of survivors, included a short speaking program, live jazz music, food, and drinks. The joyous atmosphere keeps participants coming back year after year to see fellow survivors and members of their care team who supported them through their transplant process.

CLOCKWISE FROM TOP: TRANSPLANT SURVIVORS AND THEIR FAMILIES POSTED SNAPSHOTS ON A DISPLAY BOARD AT THE EVENT; PEDIATRIC HEMATOLOGIC ONCOLOGIST FARID BOULAD WITH TRANSPLANT SURVIVOR SAMANTHA WATSON, TRANSPLANT SURVIVOR MY LUU SPOKE AT THE CELEBRATION; MEDICAL ONCOLOGIST MIGUEL-ANGEL PERALES CELEBRATED HIS PATIENTS.

Lymphoma Faculty Holiday Social 2014

THE LYMPHOMA SERVICE held its first Lymphoma Faculty Holiday Social on November 8, 2014, to celebrate the holidays and the achievements of the Lymphoma faculty. The event was attended by the entire Lymphoma faculty with their families, in addition to colleagues from the Lymphoma Disease Management Team and Heme/Onc Fellows. It was held at the RARE View Rooftop in Midtown Manhattan.

CLOCKWISE FROM UPPER LEFT: JOACHIM UAHALOM, LIA PALOMBA, ANITA KUMAR; AMANDA COPELAND, MRS. YOUNES, ALISON MOSKOWITZ; JOHN GERECITANO AND SON, JACK; NEHA MEHTA-SHAH, KATY SMITH, ERI MATSUKI

The Susan and Peter Solomon Divisional Genomics Program

THROUGH THE SUPPORT of the Peter and Susan Solomon Family Foundation, Memorial Sloan Kettering Cancer Center has pioneered efforts to develop genomics platforms to look for genetic mutations in the tumor samples of patients with different blood cancers. Our initial efforts led to rapid, cost-effective mutational studies for MSKCC patients with acute myeloid leukemia (AML), myelodysplastic syndromes, and myeloproliferative neoplasms. We have developed research-based genomic tests for all patients with hematologic malignancies and in collaboration with Foundation Medicine, we developed a state-of-the-art DNA/RNA sequencing test, which is used to comprehensively profile samples from leukemia, lymphoma and myeloma samples. This test is now being offered world-wide, and has allowed our investigators to lead the field by bringing genomic testing to the clinical setting and by defining specific roles for genomic testing in the care of patients with blood cancers.

PETER AND SUSAN SOLOMON

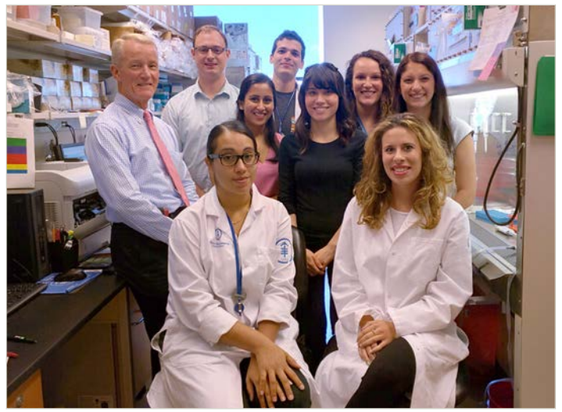
The Solomon program has also invested in new technologies that are aimed to innovate discovery and translational research in hematologic malignancies, including DNA/RNA sequencing and proteomic approaches to study blood cancers, which have allowed us to invest in our clinical/laboratory investigators and to recruit additional world leaders in blood cancer research.

Hematologic Oncology Tissue Bank

IN 2010, the Division of Hematologic Oncology established the Hematologic Oncology Tissue Bank (HOTB) to support the many different research projects of Memorial Hospital and Sloan Kettering Institute investigators.

When the bank was created in 2010, about 150 samples were processed each month. Sample processing has since increased to more than 1,020 per month. The HOTB currently has an inventory of more than 90,000 aliquots, including peripheral blood components (plasma, serum, granulocyte pellets and mononuclear cells), buccal swabs for DNA, bone marrow mononuclear cells, skin, and lymphoid tissue.

The bank is an invaluable resource for biospecimens linked to annotated clinical data, containing samples collected both before and after treatment from patients with lymphoid and hematologic malignancies.



HOTB LABORATORY MEMBERS BACK ROW, LEFT TO RIGHT: JAMES YOUNG, CHRISTOPHER FAMULARE, MINAL PATEL, NICHOLAS BROCCOLI, DIANA WIESNOSKI, CHRISTINE MALLEK, KRISTINA KNAPP; FRONT CHAIRS: KATHERINE FERRER, JULIANN ORFINI

Rekha Parameswaran, MD

ASSOCIATE ATTENDING, HEMATOLOGY SERVICE

A MULTITUDE OF FACTORS drew Rekha Parameswaran to Memorial Sloan Kettering five years ago, most notably "the chance to work at a world-class institution with amazingly smart people who are extremely dedicated to patient care."

MSK's focus on the "complete patient" is what Dr. Parameswaran, who previously served on the faculty at Tufts University in Boston, considers her own calling as well. As an associate attending physician in the Hematology Service, she treats blood-related complications stemming from cancer and its therapies and works closely with surgeons to ensure patients with all kinds of blood disorders can safely undergo complex cancer surgery. Dr. Parameswaran also conducts research on the optimal treatment and duration for cancer-related clotting problems.

In this interview, she discusses hematology treatment advances being developed at MSK, her interest in quality of care efforts, and her future goals.

How did you decide to specialize in hematology oncology?

As a second-year medical student, I studied hematology and spent hours in the laboratory looking at blood and bone marrow cells under the microscope. It was fascinating to view and learn about the delicate systems of these cells, invisible to the naked eye, where even minor changes can sometimes wreck havoc with our health. I enjoy the intellectual stimulation and the problem-solving aspect of what I do. The fact that I can bring this approach to the bedside and help patients and their families going through a very tough and vulnerable time is extremely gratifying. Even though I am just one clinician, the impact that I can have as a part of a comprehensive treatment team is gratifying.

How has your research evolved during your tenure at MSK?

Research is always a collaborative effort. As a team, Dr. Soff, Dr. Mantha and I, are trying to move forward the care of non-malignant blood disorders in the cancer setting. An important effort has been our clinical trial on Romiplostim, known commercially as Nplate®, to treat low platelet counts due to chemotherapy, known as dose limiting thrombocytopenia. If this trial proves that romiplostim is consistently successful in improving platelets counts, we will enable people to resume and continue chemotherapy to gain better control of their cancer.

Another effort from the hematology service is our quality improvement initiative to use newer targeted oral blood thinners to treat blood clots in place of standard anticoagulants, which are injectables and can pose a significant burden, on patients. As people live longer with modern cancer therapies, the goal is to have people live better. We wish to continually pursue initiatives in the supportive hematologic care arena to allow the patient enjoy a better quality of life.

What treatment advances drive home the improvements in hematology treatments today compared to even a decade or two ago?

One important thing is that cancer care itself has improved and people are living longer. Since people are then treated for longer periods, certain hematological problems can emerge more often such as the dose limiting thrombocytopenia we discussed. We are doing better at defining these problems and addressing them. Medications such as romiplostim or target specific oral anticoagulants did not even exist 20 years ago. So our armamentarium of new drugs is bigger now and will continue to evolve.

One of the things I love about working at MSK is we are always vigilant about paying attention to what patients are telling us, identifying new issues, and trying to head them off before they're a problem. That's how we push care forward.

What patient care initiatives balance out Memorial Sloan Kettering's thrust on hematologic research?

When we talk about research, we're usually thinking about the future. At the same time, we aim for the best possible patient care at the current time.

To me, what's near and dear to my heart is quality of care research into the present — how well are we doing with utilizing the tools that we already have? For example, one of our ongoing quality of care projects is focused on the process of how we take care of patients with incidentally detected blood clots at MSKCC. We have clinical algorithms in place for outpatient management of stable patients. When patients are diagnosed with a blood clot, instead of always going to the emergency room, we discuss their care with their medical oncologist, and if they are stable, they can get treated on an outpatient basis and go home. Those are care delivery and process issues that make an impact on quality of life for patients.

What excites you about your work?

I am a clinician at heart. I love taking care of patients and the relationships I develop with them. One of the toughest parts of my job is calling a patient's family when someone passes away. What excites me about working at MSK, with all the advances in cancer care here, is the hope that there will be fewer of those phone calls in the future. I would like more of our phone calls to have a happy purpose, and that's what's different about this vocation — we're helping people to lead better lives.

I also enjoy teaching and was privileged to be a recipient of an annual Fellowship Teaching Award as a hematology attending. At MSKCC we are privileged to have the brightest and best young physicians come here to pursue their training. MSKCC places a major emphasis on training the future clinical and research thought leaders. Playing a role in educating these physicians who will take the lessons learnt at MSKCC to benefit their future patients wherever they may go is another exciting aspect of my work here.

What are your future goals at Memorial Sloan Kettering?

When you are in clinic, you are making an impact on patients one at time. I want to grow that into a programmatic and systemic impact. One of the fantastic things about MSK is that we have a very robust quality assurance process in place — we're constantly looking at care delivery and processes. So part of how I want to grow my career here is along that path. Every single day, I want to make some aspect of care better.

Appointments and Promotions

GUENTHER KOEHNE PROMOTED TO ASSOCIATE MEMBER

GUENTHER KOEHNE, MD, PhD was promoted to Associate Attending Physician on the Adult Bone Marrow Transplantation Service. He received his MD and PhD from the Medical University in Hamburg, Germany. Dr. Koehne's research focuses on ways to reduce rates of disease recurrence following allogeneic stem cell transplantations, particularly how specific donor-derived immune cells (T lymphocytes) treat both the viral complications of transplantation and disease relapse following transplantation. This treatment approach has been termed "adoptive immunotherapy" and is being tested in several active clinical trials at MSK to optimize patients' outcomes.

NEHA KORDE JOINED MYELOMA SERVICE

NEHA KORDE, MD joined MSK's Myeloma Service as an Assistant Attending Physician. Dr. Korde received her MD from the University of Medicine and Dentistry of New Jersey and completed her residency in Internal Medicine at Temple University Hospital/Fox Chase Cancer Center in Philadelphia, PA. She then completed a fellowship in Hematology/Oncology at the National Institutes of Health (NIH) – National Heart, Lung, and Blood Branch. She then served as a Clinical Research Fellow/Associate Clinical Investigator at the NIH, National Cancer Institute (NCI) under Dr. Ola Landgren. Since 2009, her clinical research pursuits at the NCI has focused on multiple myeloma (MM) and transition from early precursor disease states, monoclonal gammopathy of unknown significance (MGUS) and smoldering multiple myeloma (SMM) to clinical symptomatic MM.

ANITA KUMAR JOINED LYMPHOMA SERVICE

ANITA KUMAR, MD joined MSK as an Assistant Attending in the Lymphoma Service. Dr. Kumar received her MD from the Feinberg School of Medicine, Northwestern University, and completed her residency in lymphoma at the Brigham and Women's Hospital/Harvard Medical School. She then completed a lymphoma fellowship at MSK. Dr. Kumar currently works in the Lymphoma Service and provides consultation in Hodgkin and non-Hodgkin lymphomas, as well as clinical trials of novel therapeutic agents. Dr. Kumar began clinical practice on August 18, 2014.

OLA LANDGREN JOINED MYELOMA SERVICE AS CHIEF ATTENDING

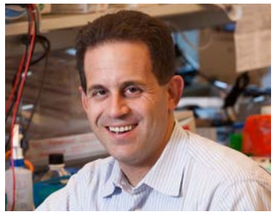
OLA LANDGREN, MD, PhD joined MSK in May 2014 as Chief Attending Physician of the Myeloma Service. He received his MD and PhD from the Karolinska Institute, where he also completed a Hematology Research Fellowship. He completed his Internal Medicine residency training at Nykoping Hospital in Stockholm. In 2004, he went to the National Cancer Institute (NCI) in Bethesda, MD as a visiting fellow and was appointed Principal Investigator in 2006 and Senior Investigator in 2011. He served as Chief of the Multiple Myeloma Section and was a Senior Investigator/Attending Physician in the Intramural Program of the NCI and Chair of The Scientific Review Committee of the Medical Oncology Branch.

Dr. Landgren has an international reputation as a clinical researcher with expertise on the molecular epidemiology and clinical management of plasma cell dyscrasias. His studies of the progression of MGUS and smoldering myeloma to clinical myeloma and the identification of high risk populations within these groups who are candidates for early intervention will be an important part of the service's research portfolio, in addition to a program of rational drug development for newly diagnosed, relapsed and refractory myeloma and amyloidosis. He is one of the pioneers in the development of minimal residual disease (MRD) testing in myeloma and will continue to develop and implement advanced MRD testing in clinical trials at MSK.

NIKOLETTA LENDVAI PROMOTED TO ASSISTANT MEMBER

NIKOLETTA LENDVAI, MD, PhD was promoted to Assistant Member on the Myeloma Service. She received her MD and PhD from the Albert Einstein College of Medicine. Her clinical research focuses on combining current treatments for myeloma (including those now in clinical trials) with immunotherapy in order to target residual disease and eliminate it, preventing relapse. In collaboration with colleagues at the Ludwig Institute for Cancer Research, she is also working to identify other cancer-testis antigens that may be suitable targets of immunotherapy either alone or in combination with the MAGE-A3 vaccine.

ROSS LEVINE PROMOTED TO MEMBER



ROSS LEVINE, MD was promoted to Attending Physician on the Leukemia Service and Member in the Human Oncology and Pathogenesis Program. He also holds the Laurence Joseph Dineen Chair in Leukemia Research. Dr. Levine was also appointed Co-Director of the Hematology-Oncology Fellowship Program in 2014. Dr. Levine received his MD from Johns Hopkins, trained in internal medicine at Massachusetts General Hospital, and was a hematology-oncology fellow at Dana-Farber Cancer Institute. He then joined Gary Gilliland's laboratory as a postdoctoral fellow and in 2007, he was recruited to MSK. He has earned Scholar Awards from the Leukemia and Lymphoma Society and the American Society of Hematology, a Young Investigator Award from the American Society of Clinical Oncology, and a Clinical Scientist Development Award from the Doris Duke Charitable Foundation.

DORIS M. PONCE PROMOTED TO ASSISTANT MEMBER

DORIS M. PONCE, MD was promoted to Assistant Attending Physician on the Adult Bone Marrow Transplantation Service. Dr. Ponce received her MD from Universidad Central de Venezuela in Caracas. She then completed an internship and residency in Internal Medicine at the Albert Einstein Medical Center in Philadelphia, PA and served as Chief Fellow in Hematology/Oncology at New York Medical College. She joined MSK in 2008 as a Fellow in the Adult Bone Marrow Transplantation Program. Her particular interest is in using cord blood as a source of blood-forming stem cells for transplantation in patients who lack a suitably matched sibling or unrelated donor, or who are in need of a urgent transplant and in the investigation of novel approaches to decrease transplant-related complications with an emphasis on graft-versus-host disease.

CRAIG SAUTER PROMOTED TO ASSISTANT MEMBER

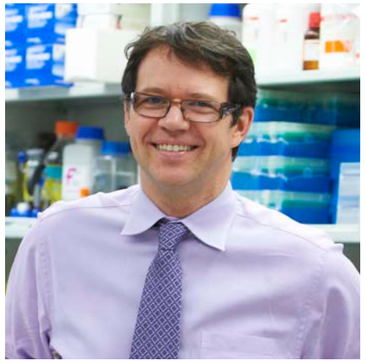
CRAIG SAUTER, MD was promoted to Assistant Attending Physician on the Adult Bone Marrow Transplantation Service. He received his MD from Case Western Reserve University and completed his residency in Internal Medicine at the University of Michigan Medical Center. He joined MSK in 2006 as a Medical Oncology/Hematology Fellow where he served as Chief Fellow from 2007-2008. His clinical expertise includes using stem cell transplantation to treat blood cancers, particularly non-Hodgkin lymphoma and chronic lymphocytic leukemia. Dr. Sauter is involved in studies that are introducing novel agents with activity against lymphoma into transplantation treatment platforms, and developing new ways to deliver cellular therapy through transplantation.

ELINA TSYVKIN JOINED LYMPHOMA SERVICE

ELINA TSYVKIN, MD joined MSK's Lymphoma Service as a Hospitalist. Dr. Tsyvkin completed her MD at Russia State University of Medicine, Moscow Institute of Medical and Social Rehabilitation in Moscow, Russia. She then completed her residency in Internal Medicine at the University of Massachusetts Medical School and a fellowship in Hematology-Oncology at Tufts Medical Center. She first joined MSK as a Neuro-Oncology Fellow from 2012-2013.

2014 Awards & Recognition

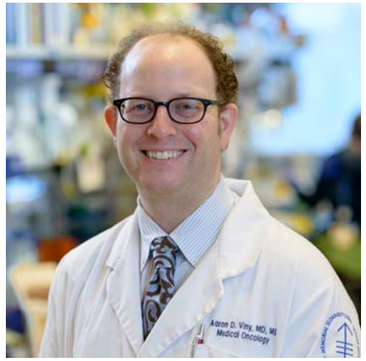
SERGIO A. GIRALT, MD



MICHEL SADELAIN, MD, PHD

RENIER BRENTJENS, MD, PHD

ALAN HANASH, MD, PHD



AARON VINY, MD

RENIER BRENTJENS received the New York Intellectual Property Law Association (NYIPLA) 2014 NYIPLA Inventor of the Year Award at a ceremony on May 20 with MSK colleague Michel Sadelain.

SERGIO A. GIRALT, Chief Attending of the Adult Bone Marrow Transplantation Service, was elected President of the American Society for Blood and Marrow Transplantation for 2014.

Dr. Giralt was also named the first incumbent of the Melvin Berlin Family Chair in Multiple Myeloma. His research focuses on improving stem cell transplant outcomes for patients with myeloma and for older patients with acute and chronic leukemia. The chair is named for Melvin R. Berlin, the founder and former Chairman of Berlin Packaging LLC.

ALAN HANASH received a $240,000 award from the Amy Strelzer Manasevit Research Program, one of the largest research grants in blood and marrow transplantation.

Dr. Hanash also received a 2014 Young Physician-Scientist Award from the American Society for Clinical Investigation.

MICHEL SADELAIN received the New York Intellectual Property Law Association (NYIPLA) 2014 NYIPLA Inventor of the Year Award at a ceremony on May 20 with MSK colleague Renier Brentjens.

AARON VINY received the 2014 American Society of Hematology (ASH) Research Training Award for Fellows.

Clinical Training and Education

PROGRAMS TRAIN THE LEADERS OF THE FUTURE

MEMORIAL SLOAN KETTERING CANCER CENTER attracts applicants from all over the world for two distinguished fellowships in Medical Oncology/Hematology and Bone Marrow Transplantation. Education in benign hematology is also provided by the Hematology Service to international medical students, internal medicine residents, and hematology/ oncology fellows.

MEDICAL ONCOLOGY/HEMATOLOGY FELLOWSHIP

Memorial Sloan Kettering's Medical Oncology/Hematology Fellowship Training Program in the Department of Medicine has a tradition of developing the careers of leading physician-scientists by providing rigorous training in the diagnosis and treatment of neoplastic disorders as well as in the conduct of clinical and/or laboratory investigation. The training program has two main objectives: to provide comprehensive training in the evaluation and care of patients with cancer, leading to board eligibility in the subspecialties of Medical Oncology or both Medical Oncology and Hematology; and to develop highly qualified and productive investigators in clinical and/or laboratory-based cancer research.

The three-year program is the largest of its kind in the country, attracting more than 450 applicants each year for just 15 coveted spots. In addition to being outstanding physicians, fellows must have a specific interest in clinical research or laboratory investigation and demonstrate scientific curiosity and motivation.

Fellows in the first year of the program concentrate on patient care, treating both inpatients and outpatients while rotating through a range of cancer subspecialties. In years two and three, fellows initiate and conduct clinical trials or work as postdoctoral researchers in a mentor's laboratory. Our fellows continue to perform world-leading research, which has led to many grant awards, impactful scientific publications, and which has allowed our fellows to become leaders in our field in their own right.

To learn more, visit http://www.mskcc.org/education/fellowships/fellowship/medical-oncology-hematology

BONE MARROW TRANSPLANTATION FELLOWSHIP

The Adult Hematopoietic Stem Cell Transplantation Fellowship Program at Memorial Sloan Kettering is an independent, one-year program designed to prepare physicians for academic careers in stem cell transplantation, including experience with clinical research. The fellowship provides training in inpatient and outpatient settings, with a specific focus on the different subspecialties within hematopoietic stem cell transplantation, as well as exposure to the different disciplines that relate to this field. These include radiation oncology and clinical laboratory rotations.

Fellows will also have opportunities to participate in ongoing research projects or to initiate an independent project. This process will be helped by the assigning of a mentor throughout the fellowship, who will ensure that the objectives of the fellow are met for the training year.

The program also includes a wide variety of conferences which complement the clinical aspects. These are based on a disease management concept and group physicians from different specialties who treat the disease in question. In addition to these patient-based conferences, a weekly research meeting is held.

To learn more, visit http://www.mskcc.org/education/fellowships/fellowship/bone-marrow-transplantation

SPOTLIGHT ON MELODY SMITH, MD

MMSAP Participant Reflects on Career-Changing Experience

AT THE 56TH ASH ANNUAL MEETING in December 2014, the Minority Medical Student Award Program (ASH MMSAP) commemorated its 10-year anniversary by highlighting Dr. Melody Smith, an MSKCC Medical Hematology/Oncology Fellow, along with other former MMSAP participants who are now pursuing careers in Hematology. Melody had been passionate about becoming a doctor since childhood but did not discover her passion for hematology and specifically bone marrow transplantation until she participated in the program.

As a first-year medical student in 2005, Melody spent her summer under the mentorship of Christopher Flowers, MD, MS, and Ned Waller, MD, PhD, at Emory Winship Cancer Institute in Atlanta, where she evaluated a strategy to reduce graft-versus-host disease (GVHD) in patients who received allogeneic bone marrow transplants (BMT). The following summer she continued her research through MMSAP and she has been researching GVHD and BMT ever since.

As a Medical Hematology/Oncology fellow at MSK, Melody researches in the lab of Marcel van den Brink, MD, PhD. Throughout the years, she has maintained contact with her ASH mentors, Drs. Flowers and Waller, and she continues to take advantage of ASH opportunities.

"My classmates often asked me how I knew so early on that I was interested in such a specific area as bone marrow transplant research," said Melody. "The fact that I started doing research as a first-year medical student through MMSAP helped me clarify that this is the field I wanted to pursue. Early exposure to hematology was key."

Swim Across America

LEFT TO RIGHT: NICOLE MAGALDI, SHANNON PETRUZELLO, DICK ENDRIS, CARMINE PETRUZELLO, JIM NORGAARD, JIM YOUNG, JEFF BODENMANN, KARA MOSESSO, NICOLE ORINGER

SWIM ACROSS AMERICA INC. (SAA) is a grassroots organization dedicated to raising money and awareness for cancer research, prevention, and treatment by sponsoring dozens of swimming events across the United States. The events unite recreational swimmers, competitive swimmers, Masters swimmers, Olympians, kayakers, boaters and hundreds of volunteers all committed to helping find a cure for cancer through athleticism, community outreach and direct service.

Since the first event was held in 1987 in Nantucket, Massachusetts, the organization has grown to hold dozens of events all over the country. Participants can swim under the Golden Gate Bridge in San Francisco, swim with NESCAC conference swimmers at Nantasket Beach, or even with Olympians in Boston Harbor. Annually, over 5,000 swimmers ranging in ages from 4 to 78, participate and there are typically 600-700 swimmers for the Long Island Sound event alone. Nationally, SAA has raised over $60 million for cancer research, prevention and treatment. One of its major research beneficiaries is Memorial Sloan Kettering Cancer Center.

Dr. James Young, an Attending Physician on the Adult BMT Service and avid distance swimmer, began swimming the Long Island Sound Open Water event in 2006. Three years later, a patient and fellow distance swimmer who had successfully recovered from an allogeneic transplant for acute leukemia proposed that they start an actual team dedicated to supporting the Adult BMT program at MSKCC. Since 2009, Team Transplant has raised over $130,000 for much needed support of the research efforts that ensure the successful use of transplantation to cure patients with leukemia, lymphoma, multiple myeloma, and other cancers of the blood and bone marrow. Team Transplant swam for its sixth year on July 26th, 2014 at the Long Island Sound Open Water Swim event. Three former patients (3, 9, and 19 yrs out from their transplants), along with one of their spouses, swam the course along with the other members of Team Transplant. Most of the team swam the 2K course, but one of the previously transplanted patients swam the 5K course and plans to swim the 10K course in 2015!

FOR MORE INFORMATION, PLEASE VISIT: www.swimacrossamerica.org.

FOR TEAM TRANSPLANT'S 2015 WEBPAGE: http://www.swimacrossamerica.org/site/TR/OpenWater/LongIslandSound/ 1330659849;jsessionid= 105866364D2450E1825AF955E5239E2A.app359b?pg= team&fr_id=3381&team_id=15872.

FOR MORE INFORMATION, PLEASE VISIT: www.cycleforsurvival.org.

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MEMORIAL SLOAN KETTERING | EQUINOX

Cycle for Survival

CYCLE FOR SURVIVAL is the national movement to beat rare cancers. The high-energy indoor team cycling events provide a tangible way for participants to fight back and 100% of Cycle for Survival funds go directly to research initiatives at MSKCC within six months of the events. To date, Cycle for Survival has raised over $76.5 million for rare cancer research and has funded over 100 clinical trials and research studies.

Jennifer and David Linn co-founded Cycle for Survival in 2007 and in 2009, it became an official MSKCC event and Equinox became the founding partner. Jennifer, who was first diagnosed with sarcoma in 2004, passed away in 2011, but her indomitable spirit and extraordinary legacy live on through Cycle for Survival.

In 2014, the Cycle for Survival national movement had several exciting firsts including kicking off the season with the Times Square Takeover ride, an appearance on "Good Morning America," ringing the Opening Bell at the New York Stock Exchange, and inaugural rides in the South and Pacific Northwest. Nearly 17,000 indoor cyclists participated in 2014 to raise $20 million at events at Equinox clubs in 13 cities: New York City, Chicago; Roslyn, Long Island; San Francisco; Los Angeles; Washington DC; Boston; Greenwich, CT; Miami; Summit, NJ; Dallas; Palo Alto; and Seattle.

PARTICIPANTS FROM THE DIVISION INCLUDED:

TEAM BMT – CYCLE 2014

CRAIG SAUTER (CAPTAIN)
KAMAL KANT SINGH ABBI
KELSEY DEAN
KATIE DRINKWATER
SHANNON DURAND
LAURA HIRSCHFIELD
NICOLE MONTANEZ
MIGUEL PERALES
SHANNON PETRUZELLO
ELAINA PRESTON
ERIN WILLIAMS

TEAM T-CELL RACERS – CYCLE 2014

HEATHER COGGINS (CAPTAIN)
NINA BAKER
KURT BANTILAN
NATASHA GALASSO
REBECCA GREEN
STEVEN HORWITZ
COLLEEN MAZZEI
SHANI MILLER
JENNA MUCHA
SUMI NAIR
STEPHEN RANDOLPH
AISHWARYA SRIRAM
KELLY THARP
JANELLE WALKLEY

LEFT TO RIGHT: KELSEY DEAN, CRAIG SAUTER, SHANNON DURAND, KATIE DRINKWATER, LAURA HIRSCHFIELD

Fred's Team Continues to Go the Distance for MSK

FRED'S TEAM is Memorial Sloan Kettering Cancer Center's athletic fundraising program that enables athletes of all abilities to fundraise directly for MSKCC by competing in marathons, half-marathons, triathlons, cycling races and other endurance events worldwide. In 2014, members raised more than $5.4 million.

On November 2, 2014, 875 Fred's Team members — including 52 Memorial Sloan Kettering staff members — ran the 26.2-mile 2014 TCS New York City Marathon, taking them through all five NYC boroughs to raise funds for the institution's lifesaving mission.

In 2014, the Division of Hematologic Oncology received nearly $51,319.32 from Fred's Team participants. Since 1995, Fred's Team has raised over $60 million.

FRED'S TEAM MEMBERS FROM THE DIVISION OF HEMATOLOGIC ONCOLOGY

KATYA AHR
MELANIE ALBANO
JANE CLANCY
CHRISTINE LIEBERTZ
HENDRIK POECK
MARCEL VAN DEN BRINK

CENTER: JANE CLANCY, CLINICAL PRACTICE MANAGER, ADULT BMT SERVICE

"My sister's best friend was an athlete. While undergoing treatment for colon cancer in 2009, I remember her telling me that she had a good day when she was able to go for a run. I realized then that if I was healthy and could run, I should take advantage of it. Every time I am running, I always think how lucky I am to be able to run."

— JANE CLANCY

Publications

These are a few articles out of the 212 total articles published by the Division of Hematology Oncology faculty in 2014.

ADULT BONE MARROW TRANSPLANTATION

Sauter CS, Matasar MJ, Meikle J, Schoder H, Ulaner GA, Migliacci JC, Hilden P, Devlin SM, Zelenetz AD, Moskowitz CH. Prognostic value of FDG-PET prior to autologous stem cell transplantation for relapsed and refractory diffuse large B-cell lymphoma. Blood. 2015 Apr 16;125(16):2579-81. PMID: 25758829

This is the first report to assess response to salvage chemotherapy by modern FDG-PET criteria prior to autologous stem cell transplantation for relapsed or refractory diffuse large B-cell lymphoma. We found that patients achieving a Deauville 1-3 response had remarkably superior outcomes in terms of progression-free and overall survival following autologous stem cell transplantation compared to patients that achieved a Deauville 4 response to salvage chemotherapy.

Ponce DM, Hilden P, Mumaw C, Devlin SM, Lubin M, Giralt S, Goldberg JD, Hanash A, Hsu K, Jenq R, Perales MA, Sauter C, van den Brink MR, Young JW, Brentjens R, Kernan NA, Prockop SE, O'Reilly RJ, Scaradavou A, Paczesny S, Barker JN. High day 28 ST2 levels predict for acute graft-versus-host disease and transplant-related mortality after cord blood transplantation. Blood. 2015 Jan 1;125(1):199-205. PMID: 25377785; PMC4281828

Cord blood transplantation (CBT) is an effective therapy for high-risk hematologic malignancies. However, up to 50% of the patients may develop a serious complication known as acute graft-versus-host disease (aGVHD) which is a leading cause of transplant-related mortality (TRM). We investigated whether protein biomarkers in the blood could predict for the development of aGVHD. We found that high levels of a biomarker known as suppressor of tumorigenicity 2 (ST2) were associated with subsequent aGVHD and increased risk of TRM. GVHD was the most common cause of death in high ST2 patients. This is the first GVHD biomarker analysis conducted in CBT recipients. These findings are currently undergoing further investigation and should facilitate future therapeutic intervention to ameliorate severe aGVHD and improve survival after CBT.

Venstrom JM, Dupont B, Hsu KC, Pittari G, Gooley TA, Chewning JH, Spellman S, Haagenson M, Gallagher MM, Malkki M, Petersdorf E. Donor activating KIR2DS1 in leukemia. N Engl J Med. 2014 Nov 20;371(21):2042. PMID: 25409391

Dr. Hsu's group continues to describe how donor immunogenetics can be leveraged to effect maximal control of leukemic relapse following hematopoietic cell transplantation (HCT). In work published in the New England Journal of Medicine, the Hsu lab describes how HLA-matched donors carrying the KIR2DS1+ gene, an activating receptor on natural killer cells, predict for beneficial outcomes in patients receiving HCT.

Purtill D, Smith K, Devlin S, Meagher R, Tonon J, Lubin M, Ponce DM, Giralt S, Kernan NA, Scaradavou A, Stevens CE, Barker JN. Dominant unit CD34+ cell dose predicts engraftment after double-unit cord blood transplantation and is influenced by bank practice. Blood. 2014 Nov 6;124(19):2905-12. PMID: 25185264; PMC4224191

This plenary paper analyzed the determinants of white cell count recovery in recipients of unrelated neonatal donor cord blood transplantation. It documented the critical importance of cord blood unit CD34+ progenitor stem cell dose and unit quality as a criteria for graft selection.

Taur Y, Jenq RR, Perales MA, Littmann ER, Morjaria S, Ling L, No D, Gobourne A, Viale A, Dahi PB, Ponce DM, Barker JN, Giralt S, van den Brink MRM, Pamer EG. The Effects of Intestinal Tract Bacterial Diversity on Mortality Following Allogeneic Hematopoietic Stem Cell Transplantation. Blood. 2014; 124(7):1174-1182. PMID: 24939656

Following bone marrow transplant, recipients with stool samples demonstrating low diversity of gut bacteria were more likely to die of transplant related causes compared to those with normal diversity. This was independent of other known predictors of mortality, suggesting the importance of the gut microbiome in this patient population.

Hubbard-Lucey VM,* Shono Y*, Maurer K, West ML, Singer NV, Ziegler CGK, Lezcano C, Motta ACF, Schmid K, Levi SM, Murphy GF, Liu C, Winkler JD, Amaravadi RK, Rogler G, Dickinson AM, Holler E, van den Brink MRM*, Cadwell K*. Autophagy gene Atg16L1 prevents lethal T cell alloreactivity mediated by dendritic cells. Immunity. 2014; 41(4):579-91. PMID: 25308334; PMC4237219.

*THESE AUTHORS CONTRIBUTED EQUALLY

These investigators discovered an unappreciated function of autophagy in dendritic cells that is critical in GVHD. They demonstrate using a well-established mouse model of allo-HSCT that Atg16L1-deficient mice are highly susceptible to lethal GVHD caused by increased T cell alloreactivity, migration of these T cells to the gut, and subsequent intestinal barrier dysfunction. This aggravated GVHD is due to a cell-intrinsic role for autophagy in preventing dendritic cell hyperactivity.

Velardi E, Tsai JJ, Holland AM, Wertheimer T, Yu VW, Zakrzewski JL, Tuckett AZ, Singer NV, West ML, Smith OM, Young LF, Kreines FM, Levy ER, Boyd RL, Scadden DT, Dudakov JA, van den Brink MRM. Sex steroid blockade enhances thymopoiesis by modulating Notch signaling. Journal of Experimental Medicine. 2014; 211(12): 2341-9. PMID: 25332287; PMC4235646

Insufficient thymic recovery has been directly correlated with increased risk of opportunistic infections and poor clinical outcomes in recipients of hematopoietic stem cell transplantation. In this paper Velardi and colleagues report that the abrogation of sex steroids, using a novel class of pharmacological inhibitors, restores the expression of the Notch ligand Delta-like 4 in thymic epithelial cells and rapidly promotes thymus regeneration and peripheral T cell reconstitution after immune injury.

LEUKEMIA

Chung SS, Kim E, Park JH, Chung YR, Lito P, Teruya-Feldstein J, Hu W, Beguelin W, Monette S, Duy C, Rampal R, Telis L, Patel M, Kim MK, Huberman K, Bouvier N, Berger MF, Melnick AM, Rosen N, Tallman MS, Park CY, Abdel-Wahab O. Hematopoietic stem cell origin of BRAFV600E mutations in hairy cell leukemia. Sci Transl Med. 2014 May 28;6(238):238ra71. PMID: 24871132

In this study, investigators from the Leukemia Service at MSKCC performed detailed genetic analyses of specimens from patients with hairy cell leukemia and also modeled this cancer in mice. Their findings unexpectedly identified the most primitive blood forming cell, the hematopoietic stem cell, as the cell of origin for what had long been thought to be a disease arising in mature B-cells. The findings from this study have significant implications for understanding the origins of and designing effective therapeutics for hairy cell leukemia and many other similar cancers.

Davila ML, Riviere I, Wang X, Bartido S, Park J, Curran K, Chung SS, Stefanski J, Borquez-Ojeda O, Olszewska M, Qu J, Wasielewska T, He Q, Fink M, Shinglot H, Youssif M, Satter M, Wang Y, Hosey J, Quintanilla H, Halton E, Bernal Y, Bouhassira DC, Arcila ME, Gonen M, Roboz GJ, Maslak P, Douer D, Frattini MG, Giralt S, Sadelain M, Brentjens R. Efficacy and toxicity management of 19-28z CAR T cell therapy in B cell acute lymphoblastic leukemia. Sci Transl Med. 2014 Feb 19;6(224):224ra25. PMID: 24553386

Our group provided the first evidence for the safety and efficacy of a novel therapy for a chemotherapy-refractory acute leukemia that is essentially fatal in adults. We demonstrated that nearly 90% of these adults can be re-induced into a complete remission, which is so dramatically effective that it suggests the first clinical indication for a engineered cell immunotherapy, designed and developed at MSKCC, is on the horizon and signals the arrival of a promising new field of cancer therapy.

Rampal R, Ahn J, Abdel-Wahab O, Nahas M, Wang K, Lipson D, Otto GA, Yelensky R, Hricik T, McKenney AS, Chiosis G, Chung YR, Pandey S, van den Brink MR, Armstrong SA, Dogan A, Intlekofer A, Manshouri T, Park CY, Verstovsek S, Rapaport F, Stephens PJ, Miller VA, Levine RL. Genomic and functional analysis of leukemic transformation of myeloproliferative neoplasms. Proc Natl Acad Sci U S A. 2014 Dec 16;111(50):E5401-10. PMID: 25516983

This study examined the frequency and spectrum of genomic alterations which occur when a chronic-phase myeloproliferative neoplasm transforms in acute myeloid leukemia. This information was then used to generate a novel murine model of leukemic transformation, which was utilized to test novel therapeutic strategies.

Rampal R, Al-Shahrour F, Abdel-Wahab O, Patel JP, Brunel JP, Mermel CH, Bass AJ, Pretz J, Ahn J, Hricik T3, Kilpivaara O, Wadleigh M, Busque L, Gilliland DG, Golub TR, Ebert BL, Levine RL. Integrated genomic analysis illustrates the central role of JAK-STAT pathway activation in myeloproliferative neoplasm pathogenesis. Blood. 2014 May 29;123(22):e123-33. PMID: 24740812; PMC4041169

This study utilized gene-expression profiling to determine if patients with the main driver mutations in philadelphia-chromoseome negative myeloproliferative neoplasm (mutations in JAK2, MPL, and CALR) have similar gene-expression signatures. The study revealed that regardless of driver mutation, activation of JAK-STAT signaling was a central feature of all MPNs examined. Notably, the presence of other co-co-occuring mutational events, such as TET2 mutations, can alter the gene-expression signature.

Bhagwat N, Koppikar P, Keller M, Marubayashi S, Shank K, Rampal R, Qi J, Kleppe M, Patel HJ, Shah SK, Taldone T, Bradner JE, Chiosis G, Levine RL. Improved targeting of JAK2 leads to increased therapeutic efficacy in myeloproliferative neoplasms. Blood. 2014 Mar 27;123(13):2075-83. PMID: 24470592; PMC3968390

In this paper we investigated the relevance of JAK2 as a therapeutic target in MPNs, and used mouse models and patient samples to show that JAK2 is not fully inhibited by current treatments and that better JAK2 inhibition can increase therapeutic efficacy. Moreover these studies demonstrated preclinical efficacy of combination JAK2/HSP90 inhibitor therapy, which is now being tested in a clinical trial on the Leukemia Service.

CONTINUED ON PAGE 32

LYMPHOMA

Moskowitz CH, Nademanee A, Masszi T, Agura E, Holowiecki J, Abidi MH, Chen AI, Stiff P, Gianni AM, Carella A, Osmanov D, Bachanova V, Sweetenham J, Sureda A, Huebner D, Sievers EL, Chi A, Larsen EK, Hunder NN, Walewski J; AETHERA Study Group. Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2015 May 9;385(9980):1853-62. PMID: 25796459

Approximately half of all Hodgkin lymphoma patients who undergo an autologous stem cell transplant will relapse. The phase 3 AETHERA trial demonstrated that approximately one year of brentuximab vedotin therapy starting early after transplant significantly improved patient outcomes compared to placebo. Based on these data and the FDA approval, brentuximab vedotin will be standard of care for classical Hodgkin lymphoma in the post-transplant consolidation setting.

Moskowitz AJ, Schöder H, Yahalom J, McCall SJ, Fox SY, Gerecitano J, Grewal R, Hamlin PA, Horwitz S, Kobos R, Kumar A, Matasar M, Noy A, Palomba ML, Perales MA, Portlock CS, Sauter C, Shukla N, Steinherz P, Straus D, Trippett T, Younes A, Zelenetz A, Moskowitz CH. PET-adapted sequential salvage therapy with brentuximab vedotin followed by augmented ifosamide, carboplatin, and etoposide for patients with relapsed and refractory Hodgkin's lymphoma: a non-randomised, open-label, single-centre, phase 2 study. Lancet Oncol. 2015 Mar;16(3):284-92. PMID: 25683846

In this manuscript we describe the results of our novel study evaluating PET-adapted therapy with brentuximab vedotin and augmented ICE chemotherapy in the pre-transplant setting for relapsed and refractory Hodgkin lymphoma. Our results show that single agent brentuximab vedotin is as effective as sequential therapy with brentuximab vedotin and combination ICE chemotherapy, provided patients achieve normalization of their PET scans before autologous stem cell transplant.

Younes A, Thieblemont C, Morschhauser F, Flinn I, Friedberg JW, Amorim S, Hivert B, Westin J, Vermeulen J, Bandyopadhyay N, de Vries R, Balasubramanian S, Hellemans P, Smit JW, Fourneau N, Oki Y. Combination of ibrutinib with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) for treatment-naive patients with CD20-positive B-cell non-Hodgkin lymphoma: a non-randomised, phase 1b study. Lancet Oncol. 2014 Aug;15(9):1019-26. PMID: 25042202

The paper established the safety and potential efficacy of combining ibrutinib with standard RCHOP chemotherapy in newly diagnosed patients with diffuse large B cell lymphoma. Based on these finding, an international randomized study comparing standard RCHOP with ibrutinib + RCHOP is being conducted.

Moskowitz AJ, Lunning MA, Horwitz SM. How I treat the peripheral T-cell lymphomas. Blood. 2014 Apr 24;123(17):2636-44. PMID: 24615779

In this article we outline how our T-cell lymphoma specialists at Memorial Sloan Kettering Cancer Center approach the management of a complex and challenging subset of non-Hodgkin lymphomas.

Ulaner GA, Lilienstein J, Gönen M, Maragulia J, Moskowitz CH, Zelenetz AD. False-Positive [18F]fluorodeoxyglucose-avid lymph nodes on positron emission tomography-computed tomography after allogeneic but not autologous stem-cell transplantation in patients with lymphoma. J Clin Oncol. 2014 Jan 1;32(1):51-6. PMID: 24248697

Following allogeneic stem cell transplantation for lymphoma, 20% (21 of 107) of patients had FDG-avid nodes up to 1.5cm in short axis on PET/CT. Biopsy of these nodes consistently demonstrated no evidence of active lymphoma. On follow up imaging, these FDG-avid nodes smaller than 1.5 cm After allo transplant, are stable or resolved. We conclude that FDG-avid that are ≤ 1.5cm nodes mimic malignancy but are benign. In comparison, auto stem cell transplant patients rarely showed FDG avid lesions that are suspicious for disease without malignant pathology.

HEMATOLOGY

Nathan H, Weiss MJ, Soff GA, Stempel M, Dematteo RP, Allen PJ, Kingham TP, Fong Y, Jarnagin WR, D'Angelica MI. Pharmacologic Prophylaxis, Postoperative INR, and Risk of Venous Thromboembolism after Hepatectomy. J Gastrointest Surg. 2014 Feb;18(2):295-302; discussion 302-3. PMID: 24129829

This was a clinical study evaluating coagulation changes and the risk of thrombosis after partial hepatectomy for primary or metastatic cancer in the liver.

Parameswaran R, Lunning M, Mantha S, Devlin S, Hamilton A, Schwartz G, Soff G. Romiplostim for management of chemotherapy-induced thrombocytopenia. Support Care in Cancer. 2014 May;22(5):1217-22. PMID: 24414994

Chemotherapy induced thrombocytopenia can cause significant delays in administration of chemotherapy. In this series, we treated 20 patients who had protracted chemotherapy induced thrombocytopenia with romiplostim, a thrombopoietin receptor agonist, and demonstrated improvement of platelet counts allowing patients to resume and maintain chemotherapy without any recurrence of dose limiting thrombocytopenia. Based on these positive results we are currently performing a clinical trial to further investigate the use of this agent in patients with dose limiting thrombocytopenia to recover their platelets and maintain chemotherapy at planned doses and schedule.

Mantha S, Sarasohn D, Ma W, Devlin SM, Chi DS, Roche KL, Suidan RS, Woo K, and Soff GA. Ovarian vein thrombosis after debulking surgery for ovarian cancer: epidemiology and clinical significance. Am J Obstet Gynecol. 2015 Mar 2. pii: S0002-9378(15)00194-5. PMID: 25743130

This is a retrospective study of ovarian vein thrombosis in patients who underwent debulking surgery for ovarian cancer at MSK over a 10-year period. We showed that ovarian vein thrombosis is commonly encountered in this setting and that anticoagulation is usually not indicated.

Mantha S, and Ansell J. Indirect comparison of dabigatran, rivaroxaban, apixaban and edoxaban for the treatment of acute venous thromboembolism. J Thromb Thrombolysis. 2015 Feb;39(2):155-65. PMID: 24989022

We compared the new oral anticoagulants using simple statistical methods and based on the landmark trials for those drugs. We found no statistically significant difference in the risk of recurrent VTE between those drugs.

MYELOMA

Ghobrial IM, Landgren O. How I treat smoldering multiple myeloma. Blood. 2014 Nov 27;124(23):3380-8. PMID: 25298034; PMC4246036

Smoldering myeloma was described in 1980; watch-and-wait has remained as the standard of care since the first case series was described. Recent and ongoing translational and clinical studies support early treatment for highrisk smoldering myeloma. This paper provides an in in-depth scientific review and discussion on the implications for modern clinical management.

Mailankody S, Korde N, Lesokhin AM, Lendvai N, Hassoun H, Stetler-Stevenson M, Landgren O. Minimal residual disease in multiple myeloma: bringing the bench to the bedside. Nat Rev Clin Oncol. 2015 May;12(5):286-295. PMID: 25622976

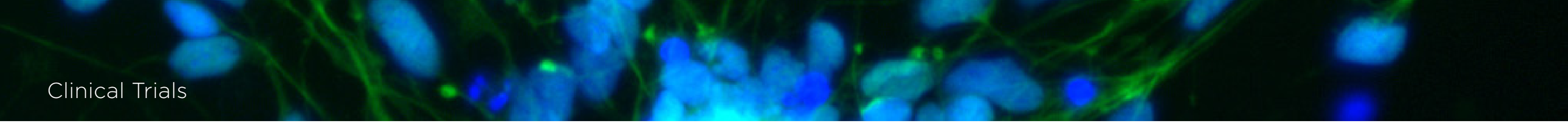
Outcomes for patients with multiple myeloma (MM) have improved substantially in the past decade, with improvements in both progression-free survival and overall survival. Many patients are now achieving a complete response to treatment, and consequently highly sensitive assays are needed for detection of minimal residual disease (MRD) in patients with MM. Results of multicolour flow cytometry and deep-sequencing studies suggest that among patients achieving a complete response, MRD-negative status is associated with significant improvements in progression-free survival and overall survival. Despite the increasing need for MRD testing in patients with MM, considerable heterogeneity in techniques for MRD detection hinders the clinical interpretation of their results. The criteria used to define MRD, strengths and weaknesses of the major types of tests (flow cytometry versus molecular testing), and the optimal sample type (bone marrow aspirate versus peripheral blood) are all unresolved dilemmas in MRD testing. This Review presents an overview of the various techniques for MRD detection in patients with MM. In addition, this article discusses challenges and opportunities for the routine use of MRD testing, possible future directions for clinical trials and implications for drug approval processes.

Ansell SM, Lesokhin AM, Borrello I, Halwani A, Scott EC, Gutierrez M, Schuster SJ, Millenson MM, Cattry D, Freeman GJ, Rodig SJ, Chapuy B, Ligon AH, Zhu L, Grosso JF, Kim SY, Timmerman JM, Shipp MA, Armand P. PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. N Engl J Med. 2015 Jan 22;372(4):311-9. PMID: 25482239; PMC4348009

The PD-1 blocking antibody, nivolumab (BMS), was tested in a signal-seeking multi-cohort phase I study in chronic myelogenous leukemia, multiple myeloma, non-Hodgkin lymphoma, and Hodgkin lymphoma. A remarkable 87% response rate was observed in 23 patients with relapsed and/or primary refractory classical Hodgkin lymphoma treated with nivolumab. The single agent activity observed in this trial lead to designation of breakthrough status by the FDA for nivolumab in patients with Hodgkin lymphoma that have failed autologous stem cell transplantation and brentuximab. Preliminary data from the remaining cohorts treated in this study was reported separately at ASH 2014.

Lendvai N, Hilden P, Devlin S, Landau H, Hassoun H, Lesokhin AM, Tsakos I, Redling K, Koehne G, Chung DJ, Schaffer WL, Giralt SA. A phase 2 single-center study of carfilzomib 56 mg/m2 with or without low-dose dexamethasone in relapsed multiple myeloma. Blood. 2014 Aug 7;124(6):899-906. PMID: 24963043

This paper described the outcomes of an investigator initiated, single center study of 44 patients with relapsed and/or refractory multiple myeloma that suggested that carfilzomib at 56 mg/m2 ± dexamethasone may provide added benefit with respect to depth of response and duration of response compared with the currently approved 20/27 mg/m2 dose of single-agent carfilzomib. Adding low-dose dexamethasone to carfilzomib may allow patients to prolong treatment, which is clinically meaningful in the advanced MM setting where salvage treatment options are limited.



Clinical Trials

These are a few highlighted clinical trials out of the 173 currently active Clinical Trials in the Division of Hematology Oncology. For more information, please visit: **https://www.mskcc.org/cancer-care/clinical-trials**.

ADULT BONE MARROW TRANSPLANTATION

A Phase I Trial of High Dose Therapy and Autologous Stem Cell Transplantation Followed by Infusion of Chimeric Antigen Receptor (CAR) Modified T-Cells Directed Against CD19+ B-Cells for Relapsed and Refractory Aggressive B Cell Non-Hodgkin Lymphoma

IRB # 12-117; PI: Craig Sauter

Given the poor outcomes of high-risk patients with relapsed and refractory diffuse large B-cell lymphoma proceeding to autologous transplantation, novel intervention is desperately needed. In this single-center phase I study we are utilizing chimeric antigen modified T-cells directed against CD19, which have demonstrated significant activity in B-cell ALL, following a standard autologous transplant with a primary safety endpoint. Preliminary data has been presented in oral abstracts at ASH and ASCO meeting and we hope to advance this study to later phase efficacy endpoints in the near future.

Autologous Stem Cell Transplant with Pomalidomide (CC-4047®) Maintenance versus Continuous Clarithromiycin/Pomalidomide/ Dexamethasone Salvage Therapy in Relapsed or Refractory Multiple Myeloma: A Phase 2 Open-Label Randomized Study by Tristate Consortium

IRB # 12-138; PI: Sergio Giralt

This trial aims to define the role of a 2nd autologous hematopoietic cell transplantation as consolidative therapy for patients with myeloma whose disease has returned after primary therapy that included an autologous hematopoietic cell transplantation. It is the only study in the country addressing this question. It is being performed through the Tristate Transplant Consortium together with Weill Cornell Medical College, State University of New York, Northshore Hospital, and Columbia University

Phase II Study of Palifermin with Leuprolide Acetate for the Promotion of Immune Recovery Following Total Body Irradiation Based T-Cell Depleted Allogeneic Hematopoietic Stem Cell Transplantation

IRB # 12-077; PI: Miguel-Angel Perales

T-cell depletion of the stem cell graft reduces the risk of graft-versus-host disease (GVHD), one of the main complications of a stem cell transplant without increasing the risk of relapse in patients with acute leukemia and MDS. One limitation, however, is a delay in recovery of the immune system and an increased risk of infections. Based on work in Dr. van den Brink's lab, this study seeks to improve immune recovery by protecting the thymus using palifermin and leuprolide.

A Randomized, Multi-Center, Phase III Trial of Calcineurin Inhibitor-Free Interventions for Prevention of Graft-versus-Host Disease (BMT CTN 1301)

IRB # 14-263; PI: Miguel-Angel Perales

Dr. Perales is the national co-Chair of this randomized phase 3 study that will seek to prove that CD34 selection of the stem cell graft (T-cell depletion) improves outcomes in patients undergoing stem cell transplant for acute leukemia or MDS by reducing the risk of chronic graft-versus-host disease (GVHD). This approach was pioneered at MSK over two decades ago and this study may change the current standard of care in the most common indications for transplant.

A Pilot Trial of a WT1 Analog Peptide Vaccine in Patients with Multiple Myeloma following Autologous Stem Cell Transplantation

IRB # 12-288; PI: Guenther Koehne

We recently described the expression of the Wilms' tumor 1 protein on malignant plasma cells. This pilot study is investigating the immunological response of a multi-valent WT1 peptide vaccine administered as post remission therapy in patients with multiple myeloma following autologous stem cell transplantation.

Phase 1/2a Study of Carfilzomib + High Dose Melphalan as Preparative Regimen for Autologous Hematopoietic Stem Cell Transplantation in Multiple Myeloma

IRB # 12-144; PI: Heather Landau

This is a phase 1/2a dose escalation study to determine the maximum tolerated dose (MTD) of carfilzomib used in combination with melphalan (200mg/m2) as conditioning prior to AHSCT for patients with relapsed multiple myeloma and carfilzomib doses up to 27mg/m2 on day-3 and 56mg/m2 on day-2 were administered safely. Additional patients are accruing in the phase 2 portion; following AHSCT, patients are randomized to two different maintenance schedules to identify a tolerable and effective maintenance regimen.

A Phase I Dose Escalation Trial of WT1-specific Donor-derived T cells following T-Cell Depleted Allogeneic Hematopoietic Stem Cell Transplantation for Patients with Relapsed/Refractory Multiple Myeloma

IRB # 12-175; PI: Guenther Koehne

This study aims at identifying tolerable, clinically active doses of Wilms' tumor protein (WT1) peptide sensitized donor-derived T cells when administered to patients with relapsed/refractory multiple myeloma following T-cell depleted allogeneic hematopoietic cell transplantation (TCD HSCT).

Myeloablative Unrelated Donor Cord Blood Transplantation with T-Cell Depleted Haplo-identical Peripheral Blood Stem Cells for Patients with High Risk Hematological Malignancies

IRB # 12-153; PI: Juliet Barker

Transplantation of neonatal cord blood has been a highly successful therapy for the treatment of high-risk cancers of the blood or bone marrow. However, while cord blood transplantation has been associated with high rates of sustained donor engraftment at MSKCC, blood count recovery is delayed. This prolonged cytopenia can result in morbidity and prolonged hospitalization, and can increase the risk of transplant-related mortality. To address this limitation, we are investigating the novel approach of the combined transplantation of a cord blood graft with CD34+ cell selected (T-cell depleted) peripheral blood stem cells from a half-matched (haplo-identical) family member. Preliminary analysis of this approach in 52 patients with hematologic malignancies has revealed that white cell count recovery is enhanced in the majority of patients. This recovery is facilitated by early engraftment of the related donor. However, rejection of the related donor by the cord blood graft is universal and this process has been associated with sustained leukemic remission in many patients with aggressive disease. Investigation of the biology and determinants of survival after this novel therapy is ongoing.

LEUKEMIA

A Phase I Trial of Precursor B Cell Acute Lymphoblastic Leukemia (B-ALL) Treated with Autologous T Cells Genetically Targeted to the B Cell Specific Antigen CD19(CAR)

IRB # 09-114, PI: Jae Park

Our group has been leading the effort to investigate the safety and efficacy of autologous T cells genetically modified to express chimeric antigen receptor targeting the B cell specific antigen, CD19. Using these CD19-targeted CAR modified T cells, we have treated over 40 adult patients with relapsed B-ALL and observed a complete response rate of 87-90%. Since adults with relapsed or refractory B-ALL have dismal prognosis with currently available conventional chemotherapy, the CAR T cells represent a novel therapeutic approach with promising anti-tumor efficacy and may provide a framework for future immunotherapy in hematologic malignancies.

A Phase 1, Multicenter, Open-Label, Dose-Escalation, Safety, Pharmacokinetic, Pharmacodynamic, and Clinical Activity Study of Orally Administered AG-221 in Subjects with Advanced Hematologic Malignancies with an IDH2 Mutation

IRB # 13-154, PI: Eytan Stein

AG-221 is a small molecule inhibitor that blocks the action of mutated IDH-2, an abnormality found in about 15% of patients with acute myeloid leukemia (AML). To date, the results of this phase 1, dose escalation and dose expansion trial have been remarkable. The overall response rate of this very poor risk patient population is 40%, with many patients achieving a complete remission. The study is ongoing and entering a second dose expansion phase to look more closely at the efficacy of AG-221 in a patients with relapsed and refractory AML.

A Phase 1, Open-Label, Dose Escalation and Expanded Cohort, Continuous Intravenous Infusion, Multicenter Study of the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of EPZ-5676 in Treatment Relapsed/Refractory Patients with Leukemias Involving Translocations of the MLL Gene at 11q23 or Advanced Hematologic Malignancies

IRB # 12-181, PI: Martin Tallman

Abnormalities in chromosome 11q23 are often seen as a result of treatment for other cancer in leukemia patients, and have a poor prognosis. EPZ-5676 is a small molecule inhibitor that blocks the action of an enzyme called DOT1L that is thought to be intricately involved in the development and maintenance of these leukemias. The trial is currently in a dose expansion phase to get further experience with the safety and efficacy of this agent.

A Phase II Study of the BRAF Inhibitor, Vemurafenib, in Patients with Relapsed or Refractory Hairy Cell Leukemia

IRB # 12-200, PI: Jae Park

HCL is characterized by nearly 100% frequency of the BRAFV600E mutation that is the key driver in HCL development. We investigated the efficacy of the BRAF inhibitor, vemurafenib, in relapsed HCL by conducting the first U.S. multicenter, investigator-initiated, phase II clinical trial. We have enrolled 26 patients with relapsed HCL, and observed 100% overall response rates (CR+PR) in this refractory patient population. While longer follow up is needed to confirm the durability of response, this trial provides a proof-of-concept and validates mutant BRAF as a rational therapeutic target in HCL.

CONTINUED ON PAGE 36

A Novel "Pediatric-Inspired" Regimen with Reduced Myelosuppressive Drugs for Adults (aged 18-60) with Newly Diagnosed Ph Negative Acute Lymphoblastic Leukemia

IRB # 12-266, PI: Dan Douer

ALL, although rare, is the most common cancer in children with 80% cure rate, yet half of ALL patients are older than 20 years old and only half of them are cured. For decades, pediatricians and oncologist who treat adults have independently developed fundamentally separate treatment chemotherapy approaches for newly diagnosed ALL. Such dramatic difference in treatment occurring at age 20-21 years is odd, without medical rational, and in a historic perspective probably wrong. We adopted a chemotherapy regimen following pediatric principals including multiple doses of asparaginase — a drug that was minimally used in adults — into a clinical trial for adults with Philadelphia negative ALL. With several minor modifications and very tight safety measures for monitoring and managing asparaginase toxicity, our treatment is safe at least until age 50-60 years. We are also noticing an overall lower relapse rate and in more than half of those who respond fast (within 4 weeks) as identified by advanced laboratory technology, relapses are rare without transplantation. In collaboration with our basic scientists we are exploring genetic aberrations in the leukemia cells to better identify those who are not likely to respond and refer them to novel experimental treatments based on their abnormal genetic structure.

LYMPHOMA

A Phase Ib/II, Open-Label Study Evaluating the Safety and Pharmacokinetics of GDC-0199 (ABT-199) in Combination with Rituximab (R) or Obinutuzumab (G) Plus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) in Patients with B-cell Non-Hodgkin's Lymphoma (NHL) and DLBCL

IRB # 14-130, PI: Andrew Zelenetz

To estimate the maximum tolerated dose for venetoclax (ABT-199, GDC-0199) in combination with R-CHOP or Obinutuzumab (GA-101) + CHOP to treat previously untreated or relapsed/refractory patients with NHL (excluding mantle cell lymphoma). After establishing a recommended phase 2 dose, a cohort of previously untreated DLBCL patients will be evaluated to assess the efficacy of the combination of venetoclax with either R-CHOP vs G-CHOP. The assessment of efficacy will be used to guide further development of the combinations.

A Phase Ib Multi-Cohort Trial of MK-3475 in Subjects with Hematologic Malignancies

IRB # 13-220, PI: Craig Moskowitz

This Phase 1 study of the PD-1 inhibitor pembrolizumab in heavily pre-treated patients with Hodgkin lymphoma. All patients in this study failed previous treatment with brentuximab vedotin, and 67 percent of those patients had relapsed after a stem cell transplant. Treatment was extremely well tolerated and 80% of patients had clinical benefit. It is very likely this agent will be approved for the treatment of patients with Hodgkin lymphoma

Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Multiple Dose Regimens of MT-3724 for the Treatment of Patients with Relapsed Non-Hodgkin's B-Cell Lymphoma

IRB # 14-265, PI: Paul Hamlin

In 2014 we initiated a Phase I study investigating a novel immuno-toxin conjugate named MT-3724 (Molecular Templates Pharmaceutical) in relapsed/refractory NHL. This agent represents an exciting new therapy with the promise of delivering a unique mechanism of cell kill via a Shiga-like toxin paired with the specificity of antibody-like targeting to CD20. Enrollment is ongoing in 2015.

A Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, PCI-32765 (Ibrutinib), in Combination with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Subjects With Newly Diagnosed Non-Germinal Center B-Cell Subtype of Diffuse Large B-Cell Lymphoma

IRB # 13-146, PI: Anas Younes

This international randomized study comparing standard RCHOP with ibrutinib + RCHOP is being conducted based on the findings of the paper titled, "Combination of ibrutinib with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) for treatment-naive patients with CD20-positive B-cell non-Hodgkin lymphoma: a non-randomised, phase 1b study" published in Lancet Oncology in August 2014.

A Phase 1b, Open-label, Multicenter Study of Urelumab (BMS-663513) in Combination with Rituximab in Subjects with Relapsed/Refractory B-Cell Malignancies

IRB # 13-252, PI: Andrew Zelenetz

Urelumab (anti-41BB, anti-CD137) has pleotropic effects on the immune microenvironment with a net effect of enhancing T cell and NK cell function. This study is to evaluate the safety of urelumab in combination with rituximab to treat B cell NHL patients and get a preliminary determination of efficacy. The study includes correlative assays to determine the impact of urelumab on the immune microenvironment in vivo. The goal is to determine if there is adequate safety and tolerability that permits further clinical testing.

HEMATOLOGY

A Randomized Open Label Phase II Study of Romiplostim Versus Observation for Chemotherapy Induced Thrombocytopenia

IRB # 13-132, PI: Gerald Soff

This is an ongoing clinical trial of romiplostim for treatment of chemotherapy-induced thrombocytopenia.

MYELOMA

VLX1570 and Low-Dose Dexamethasone in Relapsed or Relapsed and Refractory Multiple Myeloma: A Clinical and Correlative Phase 1/2 Study

IRB # 14-274; PI: Ola Landgren

Proteasome inhibition is one of the most effective targets for the treatment of multiple myeloma. This first-time-in-man phase 1/2 clinical trial with Dr. Landgren as the lead-PI uses a novel approach to inhibit the 19S proteasome upstream of current 20S proteasome inhibitors (e.g., velcade, carfilzomib). Preclinical data show strong effect in velcade resistant myeloma cell lines.

A Randomized Phase III Study Comparing Conventional Dose Treatment Using a Combination of Lenalidomide, Bortezomib and Dexamethasone (RVD) to High-Dose Treatment with Peripheral Stem Cell Transplant in the Initial Management of Myeloma in Patients Up to 65 Years of Age

IRB # 12-018; PI: Hani Hassoun

First line treatment for younger patients with multiple myeloma has included, after an initial induction therapy, autologous stem cell transplantation (ASCT). This treatment paradigm has been considered "standard of care" since the 1990s when clinical trials have established the benefit of incorporating ASCT in first line therapy. However, many new drugs have been developed since the 1990s. Therefore, this clinical trial is questioning the role of ASCT in first line therapy in the era of new agents. This randomized phase III trial compares continuous treatment with new agents versus the standard approach that incorporates ASCT. This is a large multicenter national trial which will be able to answer this question and possibly be practice changing.

Phase II Study of Infusional Carfilzomib in Patients with Relapsed or Refractory Multiple Myeloma

IRB # 10-228; PI: Nikoletta Lendvai

This is an investigator initiated, single center study of 44 patients with relapsed and/or refractory multiple myeloma that suggested that carfilzomib at 56 mg/m2 ± dexamethasone may provide added benefit with respect to depth of response and duration of response compared with the currently approved 20/27 mg/m2 dose of single-agent carfilzomib. Adding low-dose dexamethasone to carfilzomib may allow patients to prolong treatment, which is clinically meaningful in the advanced MM setting where salvage treatment options are limited.

A Phase I Open Label Dose Escalation and Randomized Cohort Expansion Study of the Safety and Tolerability of Elotuzumab (BMS-901608) Administered in Combination with either Lirilumab (BMS-986015) or Urelumab (BMS-663513) in Subjects with Multiple Myeloma

IRB # 14-206; PI: Alexander Lesokhin

This is a phase I trial investigating if modulating natural killer (NK) cell mediated antibody dependent cytotoxicity (ADCC) can enhance the efficacy of a monoclonal antibody directed at the myeloma tumor antigen CS1. Elotuzumab, an antibody against CS1 that has limited single agent activity in patients with relapsed multiple myeloma is being combined with either lirilumab, an antibody that releases the brakes on NK cells by blocking a family of inhibitory receptors (KIR2DL1/2/3), or urelumab, an anti-CD137 agonist antibody that can enhance the activation of both NK and CD8 T cells. Patients with either relapsed/refractory multiple myeloma or minimal residual disease detected following autologous stem cell transplant are eligible.

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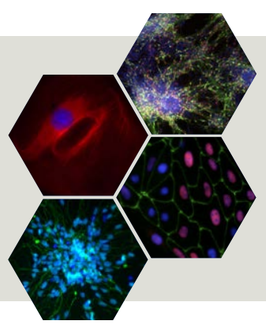

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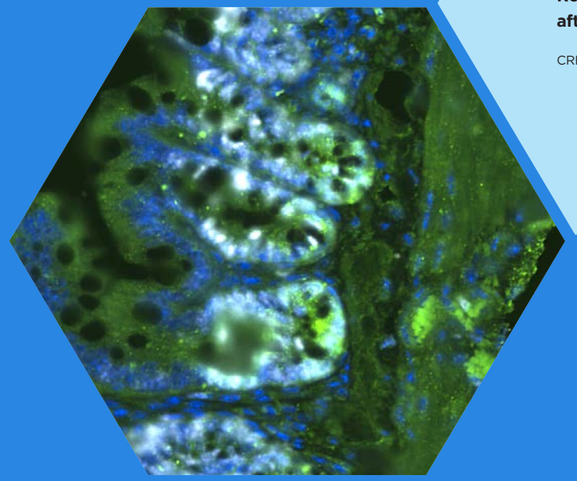

FOCUS ON

Regenerating intestinal stem cells after bone marrow transplant

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