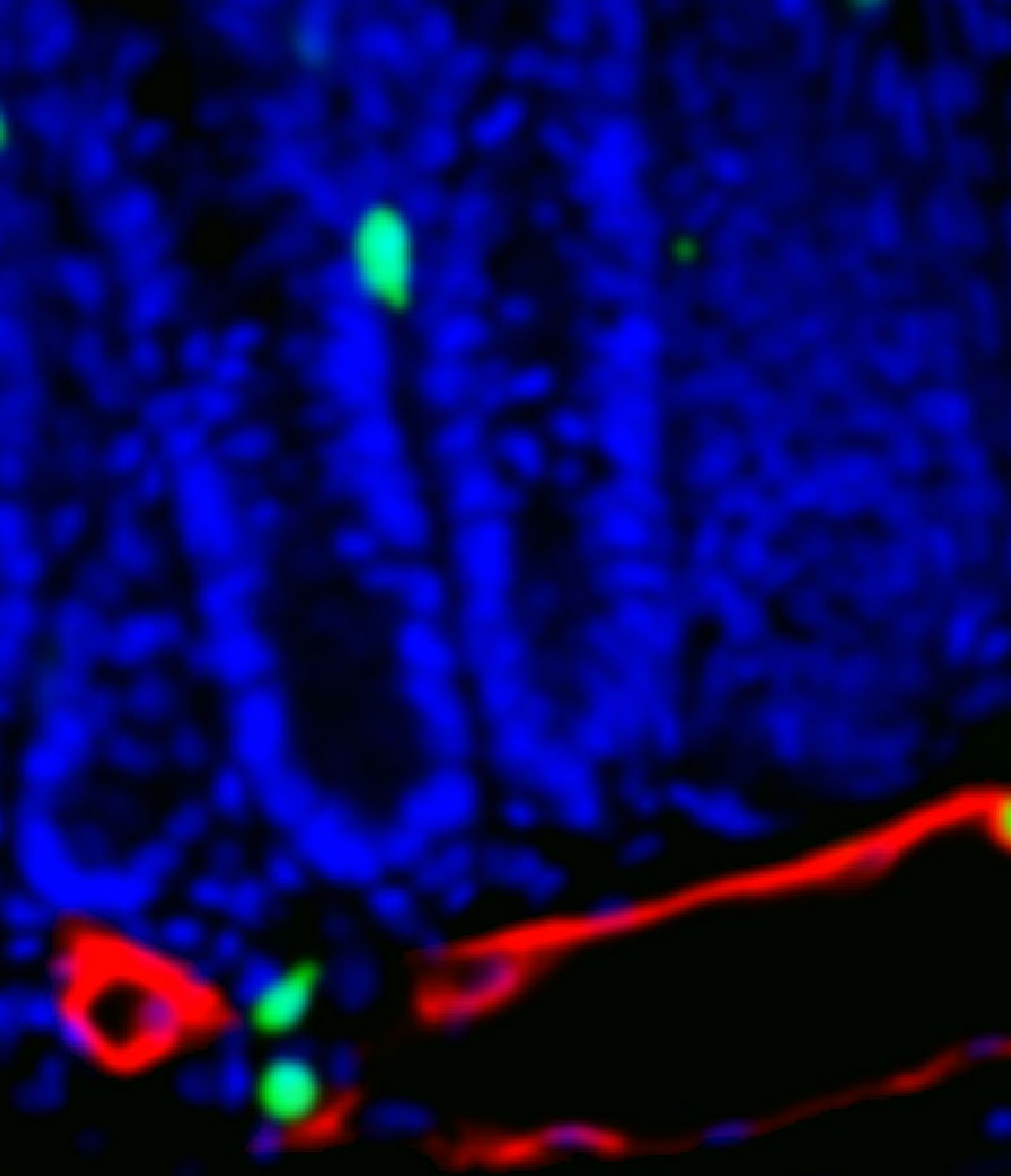
DIVISION OF HEMATOLOGIC MALIGNANCIES

2018 Annual Report

Memorial Sloan Kettering Cancer Center



This 2-D optical image shows the migration of donor T cells (green) from blood vessels (red) to the intestinal crypts after bone marrow transplantation in a clinically relevant graft-versus-host disease.
Source: Alan Hanash lab

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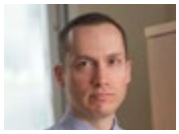
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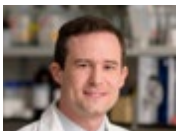
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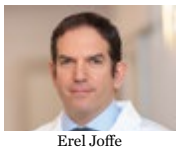
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AREAS OF COLLABORATION

Cardiology
Case Management
Colorectal
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Gastric & Mixed Tumor
Gastroenterology & Nutrition
General Internal Medicine
Geriatrics
Gynecology
Head & Neck
Hepatopancreatobiliary
Infectious Diseases
Integrative Medicine
Interventional Radiology
Laboratory Medicine and Cell Therapy
Music/Art Therapy
Neurology
Neurosurgery
Nursing
Nutrition
Occupational Therapy
Ophthalmic Oncology
Orthopaedic Service
Pain & Palliative Care
Pathology
- Cytology
- Hematopathology
- Molecular Pathology

Physical Therapy
Plastic & Reconstructive Surgery
Psychiatry
Pulmonary
Radiation Oncology
Radiology
Rehabilitation Medicine
Renal
Social Work
Surgery
Surgical Pathology Diagnostic Services:
- Bone & Soft Tissue
- Dermatology
- Gastrointestinal

Thoracic
Urgent Care
Urology

LETTER FROM THE DIVISION HEAD

Marcel van den Brink, Head of the Division of Hematologic Malignancies (left), with hematologic oncologist Melody Smith (right)

Hematologic oncologist Aaron Viny, and his daughter, Lilah, at Cycle for Survival

The division participated in the Lemons for Leukemia challenge.

We are happy to share the progress of the Division of Hematologic Malignancies in the Department of Medicine at Memorial Sloan Kettering Cancer Center.

Our program continues to grow in all areas of clinical care, research (both clinical and laboratory-based) and education. At the present time, it consists of 83 physicians all devoted to the care of patients with blood cancers. These physicians work in close collaboration with other physicians, nurses, pharmacists, advanced practice providers, administrators, and many others.

In this annual report, we will cover some exciting accomplishments in the division ranging from gut microbes to novel drugs for leukemia. But more importantly, we want you to meet some of the amazing members of our team.

- Anthony Mato, Director of the Chronic Lymphocytic Leukemia Program
- Ola Landgren, Chief of the Myeloma Service; Donna Mastey, Clinical Trials Nurse III; and Natasha Jafri, Clinical Research Manager
- Steven Horwitz, Attending in the Lymphoma Service
- Valkal Bhatt, Clinical Pharmacy Specialist III in the Adult BMT Service
- Anne Marie Gonzales-Dadiz, Research Program Manager in the Clinical Trials Office
- Elizabeth Schmidt Rodriguez, Nursing Director at the David H. Koch Center for Cancer Care
- Thea Novick, Associate Director of Development Programs

Sincerely,

Marcel van den Brink, MD, PhD
Alan N. Houghton Chair in Immunology
Head, Division of Hematologic Malignancies
Memorial Sloan Kettering Cancer Center

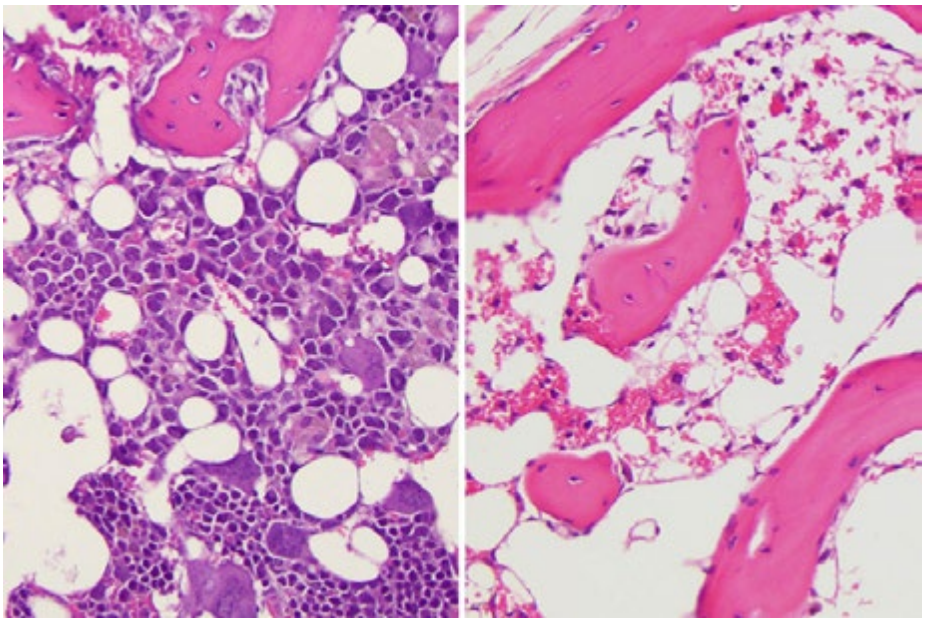
GUT MICROBES HELP FEED A REGROWING IMMUNE SYSTEM AFTER A BONE MARROW TRANSPLANT

By Matthew Tontonoz

Antibiotics are often necessary to prevent infection after a bone marrow transplant (BMT). But they can also disrupt the body's natural ecosystem of microbes. A recent study examined what gut microbes provide to a regrowing immune system.

For people with blood cancer, a BMT can be a lifesaving treatment option. But the procedure can have dangerous side effects, including an increased susceptibility to infections during the time it takes for the bone marrow to produce new immune cells. As a result, BMT patients must receive antibiotics as a precaution.

Research from the lab of Sloan Kettering Institute immunologist Marcel van den Brink, Head of the Division of Hematologic Malignancies at Memorial Sloan Kettering, suggests ways to improve immune system recovery after a BMT.



Antibiotic treatment that depletes gut flora slows down the regrowth of immune cells in the bone marrow. Mice with disrupted gut flora showed very little regeneration of immune cells (right) compared with animals with intact gut flora (left).

HINT: TRUST YOUR GUT

The researchers used a mouse model of bone marrow transplantation to examine the relationship between antibiotics and immune system recovery. They found that the immune system was slower to regrow in antibiotic-treated animals, compared with animals that did not receive antibiotics. The difference, they discovered, was due to a reduction in the number and diversity of gut microbes — what scientists call the intestinal microbiota — in the antibiotic-treated mice.

MICROBES: THEY DO A BODY GOOD

What might gut microbes have to do with a regrowing immune system? These microscopic residents do many things for the animals they live inside. One important job is helping their hosts obtain nutrition from the foods they eat. This nourishment, it turns out, is also key for repairing the immune system after a BMT, and the antibiotic-treated mice weren't getting enough.

But there was a simple fix: The team discovered that the effect of a depleted microbiota could be offset by supplementing the mice's drinking water with a little bit of sugar (equivalent to about 7 percent of a mouse's average daily calories).

"That a seemingly small and simple intervention can improve immune recovery after a bone marrow transplant was quite striking to me," says Anna Staffas, a postdoctoral fellow in the van den Brink laboratory and the first author of a paper on the study, which was published in the journal *Cell Host and Microbe*.

"That a seemingly small and simple intervention can improve immune recovery after a bone marrow transplant was quite striking to me."

Anna Staffas
Postdoctoral Fellow

The results suggest that people receiving a BMT might benefit from nutritional or dietary changes that help compensate for the loss of intestinal microbiota following treatment with antibiotics.

Dr. van den Brink's lab had previously shown that the types of antibiotics a person receives after a BMT, and the diversity and extent of their gut flora, can influence how well they do after a BMT. This latest research extends the role of gut flora to providing key nutritional benefits that support immune recovery.

MSK is currently conducting clinical trials to test a variety of nutritional strategies to boost immune system recovery in people who receive a BMT. ■

This work was supported by the National Institutes of Health; the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Institute of Allergy and Infectious Diseases; the National Institute of Diabetes and Digestive and Kidney Diseases; the Lymphoma Foundation; the Susan and Peter Solomon Divisional Genomics Program; the Parker Institute for Cancer Immunotherapy at Memorial Sloan Kettering Cancer Center; the Cancer Prevention and Research Institute of Texas; Seres Therapeutics; the Swedish Research Council; the Swedish Society for Medical Research; and the Swedish Society of Medicine. Dr. van den Brink is a member of the scientific advisory board at Seres Therapeutics.

REDUCING TOXICITIES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

By Michael Scordo and Miguel-Angel Perales

Despite significant advances in supportive care and improvements in allogeneic hematopoietic stem cell transplantation (HCT) outcomes, about one in every three patients succumbs to post-transplant toxicities, half of which are not related to graft-versus-host disease (GVHD).

While the use of ex vivo CD34$^+$-selected stem cells for an HCT significantly reduces the risk of both acute and chronic GVHD, and eliminates the need for post-transplant immunosuppressive drugs, reducing the post-transplant toxicity burden remains a focal point in research to improve patient outcomes.

CD34 is expressed on hematopoietic progenitor cells found in bone marrow and cord blood. CD34$^+$ stem/progenitor cells are multipotent and can give rise to all cell types in blood.

Memorial Sloan Kettering, one of the pioneers of myeloablative HCT with ex vivo CD34$^+$-selected stem cells, has ongoing research efforts to characterize toxicities and identify risk factors that impact morbidity and mortality in adults undergoing this approach.

In three recent papers published in the *Biology of Blood and Marrow Transplantation*, we categorize the numbers and types of specific organ toxicities following CD34$^+$-selected transplantation and describe the predictive factors.

Overall, we found that pretransplantation cytomegalovirus (CMV), seropositivity, and a higher ferritin level were associated with poorer outcomes, while a pretransplantation higher absolute lymphocyte count and increased albumin level were associated with improved outcomes.

MINIMIZING TOXICITIES WITH CD34$^+$-SELECTED STEM CELLS

Managing the efficacy of intensive pretransplant conditioning and the graft-versus-tumor effect while minimizing the effects of GVHD and nonrelapse mortality is a challenging balancing act for clinicians treating patients undergoing allogeneic hematopoietic stem cell transplantation.

The current standard regimen to control GVHD is the administration of immunosuppressive agents — most commonly, the calcineurin inhibitors tacrolimus (Astagraf XL®, Envarsus XR®, Prograf®) and cyclosporine (Gengraf®, Neoral®, Sandimmune®) — together with methotrexate (Rheumatrex®, Trexall®). This regimen, referred to as Tac/MTX, is administered for the first six to nine months after transplantation. While Tac/MTX can control acute GVHD well, it is less effective at managing chronic GVHD and may produce toxicities and side effects.

The use of ex vivo CD34$^+$-selected stem cells involves depleting donor T cells from the graft. This approach has demonstrated significantly reduced acute and chronic GVHD while maintaining good outcomes in people with acute leukemia or myelodysplastic syndrome in complete remission. The approach eliminates the need to treat people with Tac/MTX post-transplantation and, accordingly, eliminates Tac/MTX-associated toxicities from occurring. However, people receiving CD34$^+$-selected stem cells still require pretransplant myeloablative conditioning, which can influence the range of toxicities they experience post-transplant.

Memorial Sloan Kettering, one of the pioneers of myeloablative HCT with ex vivo CD34$^+$-selected stem cells, has ongoing research efforts to characterize toxicities and identify risk factors that impact morbidity and mortality in adults undergoing this approach.

RECENT LEARNING FROM MSK PATIENTS

Memorial Sloan Kettering is one of 27 centers participating in the ongoing Blood and Marrow Transplantation Clinical Trials Network randomized, controlled phase III trial BMT CTN 1301, NCT0234580, co-chaired by Miguel-Angel Perales from MSK. The study is comparing two calcineurin inhibitor–free strategies for reducing GVHD in 345 patients randomized to three treatment groups: CD34$^+$-selected stem cells with the CliniMACs CD34 Reagent System, bone marrow transplant followed by post-transplantation cyclophosphamide, and bone marrow transplant followed by standard Tac/MTX treatment.

While this large prospective trial is ongoing, we analyzed electronic health record data for adult MSK patients who had been enrolled in previous trials at MSK and treated with CD34$^+$-selected stem cell transplants. We identified toxicities and associated risk factors and their impact on outcomes for three subgroups: first-year survivors, longer-term survivors, and adults over the age of 60. Our findings for each subgroup are as follows:

One-Year Outcomes: The first study examined the impact of grade 3 or higher toxicities on first-year outcomes in 200 adults ages 19 to 73 years (median age 57 years). Overall, this group experienced low rates of acute GVHD, in contrast to conventional transplants with myeloablative conditioning; low rates of sinusoidal obstruction syndrome; and good rates of nonrelapse mortality, progression-free survival, and overall survival. By the 100-day milestone, only six patients (3 percent) had developed grade 3 and 4 GVHD. One-year post-transplantation, 149 of 200 patients (75 percent) were alive. Of the 51 who had died, 17 died of disease whereas twice as many, 34, died of nonrelapse mortality.

Patients experiencing pulmonary, renal, hepatic, and neurological toxicities had an increased risk of death and nonrelapse mortality. Our analysis revealed that CMV-positive patients who developed pulmonary and renal toxicities experienced a higher risk of poorer outcomes in the first year. High ferritin pretransplantation was significantly associated with serious hepatic complications. We also found that patients who had a higher level of busulphan than planned also had worse outcomes.

Longer-Term Outcomes: In a second study, we analyzed late adverse effects among 131 patients who survived more than one year post-transplantation (median follow-up time of 36 months). Four-year overall survival for patients who survived one year was strong at 77 percent. The development of grade 3 or higher toxicities in the first year was associated with poorer outcomes, emphasizing the need for early identification and intervention strategies when toxicities arise.

Among all of the toxicities recorded, 75 percent occurred within two years of

Miguel-Angel Perales, Deputy Chief of the Adult Bone Marrow Transplant Service with a patient

transplantation. Cardiovascular, hematologic, hepatic, infectious, metabolic, neurologic, and pulmonary toxicities that occurred one year post-transplantation were independently associated with poorer outcomes, even after adjusting for higher scores using the Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI) pretransplantation and whether patients developed grades 2 through 4 acute GVHD within the first year of receiving transplants.

Pretransplantation absolute lymphocyte count greater than 500 cells per cubic millimeter and serum albumin greater than 4.0 grams per decilitre were associated with reduced risks of developing hematologic, infectious, metabolic, and pulmonary toxicities, as well as a reduced risk of death and nonrelapse mortality. Serum ferritin greater than 1,000 nanograms per millilitre was associated with a higher risk of toxicities and nonrelapse mortality after one year.

Older Adults: In the third study, we examined the impact of toxicity on survival outcomes for older patients and compared results for 80 patients over 60 years with 120 patients ages 18 to 59 years.

Overall survival and nonrelapse mortality were similar between patients over and under 60 years of age, with a one-year overall survival rate of 70 percent versus 78 percent ($p=.07$) and a one-year nonrelapse mortality rate of 23 percent versus 13 percent ($p=.38$), respectively. These results suggest that many older patients who undergo allogeneic hematopoietic cell transplantation have favorable outcomes.

Patients in the older group had a higher risk of neurologic and cardiovascular toxicities but a lower risk of oral and gastrointestinal issues compared with those in the younger group. Overall, cardiovascular, hepatic, neurologic, pulmonary, and renal toxicities were independent risk factors for death and nonrelapse mortality, after controlling for higher comorbidity scores pretransplantation.

CMV seropositivity in this patient group was associated with the development of several toxicities, suggesting that further research about the impact of CMV status is warranted.

Few studies have systematically characterized specific organ toxicities after allogeneic hematopoietic stem cell transplantation. Our findings in these three recently published papers suggest that simple blood tests for CMV, ferritin, absolute lymphocyte count, and albumin may complement widely used prognostic tools, such as the HCT-CI, for risk assessment in people receiving myeloablative allogeneic hematopoietic stem cell transplantation with ex vivo $CD34^+$-selected stem cells. Earlier identification of toxicities and developing timely intervention strategies will help more people achieve better, longer-term outcomes in the future.

At MSK, we treat hematologic cancers with advanced expertise and multidisciplinary collaboration. As leaders in the field, we are committed to pioneering advances in stem cell transplants that can reduce the risk of disease relapse, as well as the potential toxicities and symptom burden associated with bone marrow and stem cell transplantation in order to achieve the best possible outcomes for our patients.

In April 2018, we convened the "International Symposium on Hematopoietic Cell Transplantation-Related Toxicities." This symposium brought together thought leaders and participants from around the world in the fields of hematopoietic cell transplantation and related medical subspecialties. Speakers discussed mechanisms of toxicities and symptom burden after hematopoietic cell transplantation that are not related to graft-versus-host disease in order to identify best practices to both prevent and treat these complications. Over the two-day symposium, speakers and attendees also met in dedicated breakout sessions that facilitated collaborative efforts in planning future research aimed at mitigating serious toxicities, reducing symptom burden, and improving patients' outcomes. ■

Ross Levine determined the connection between clonal hematopoiesis and blood cancer.

MSK OPENS A NEW CLINIC TO MONITOR PEOPLE WITH A GENETIC RISK FOR DEVELOPING BLOOD CANCER

By Julie Grisham

The clinic will focus on clonal hematopoiesis (CH). This age-related condition increases the risk of developing certain blood cancers.

Most cancers arise by chance and, therefore, are hard to predict. But scientists and doctors are learning more about the genetic changes that cause cancer as well as those that signal a higher risk for it. Thanks to MSK-IMPACT™, Memorial Sloan Kettering's diagnostic test that looks for genes associated with cancer, more people who carry cancer-related genes are being identified.

To take advantage of these new opportunities, MSK has launched the Precision Interception and Prevention Initiative. This program is focused not only on catching cancer very early but also on eventually preventing it from forming in the first place. One of the program's components is a clinic for people with CH. MSK's clinic, the first of its kind, began to see people with CH in early 2018.

"This initiative unites high-impact science and clinical medicine to actively identify and help a population of people who are either at a high risk of developing cancer or who already have cancer but don't know it," says Luis Diaz, Head of MSK's Division of Solid Tumor Oncology, who is leading this effort.

A person with clonal hematopoiesis has an increased number of blood cells that carry some of the same mutations that are found in blood cancers. CH occurs when hematopoietic stem cells (which give rise to all types of blood cells) form cells that are genetically distinct from the rest of the blood stem cells. Sometimes these distinct cells carry cancer-associated mutations.

"This is an exciting and quickly growing field, and it's vital for us to learn as much about it as possible," says physician-scientist Ross Levine. "By launching this effort to monitor and care for people with CH, we will be able to advance our understanding about this important area of science."

CLONAL HEMATOPOIESIS: A COMMON PHENOMENON LINKED TO AGING

Dr. Levine was part of the research team that first identified the genetic basis of CH and its connection to blood cancer. They first reported that relationship in 2012. Since then, many investigators have begun to study the condition and have shown that CH is very common. Researchers have found that it is linked to an increased risk of certain blood cancers, especially myelodysplastic syndrome and acute myeloid leukemia, as well as cardiovascular disease, heart attacks, and strokes.

The most common cause of CH is aging. Studies have suggested that between 10 and 20 percent of people over age 70 have signs of it in their blood. Smoking also increases the risk. "CH is very common. Millions of people have it," Dr. Levine says. "But most people don't know they have it, and doctors don't know what to do with it. We thought it was important to do more research on this phenomenon so that we can start figuring out who may need intensive follow-up and treatment right away and who can be observed."

"Right now we don't have good ways to predict who is most likely to develop a blood cancer, so any new findings that come out of this clinic have the potential to make a big difference," says Marcel van den Brink, Head of MSK's Division of Hematologic Malignancies.

In addition, certain types of chemotherapy and radiation therapy can increase the incidence of CH. This explains why cancer survivors carry a risk for secondary leukemia. The still-rare condition is happening more often because more people with cancer are surviving longer or are cured of their disease.

A study last year from Dr. Levine, MSK researcher Michael Berger, and their colleagues found that 25 percent of people with any type of cancer had CH, a higher number than had previously been observed. Of that group, 4.5 percent had specific mutations that are known to drive the formation of leukemia.

TREATING BLOOD CANCER EARLIER

Most people with CH will never develop blood cancer, but doctors are starting to understand which individuals with CH are at the highest risk. "This is one of the reasons this clinic is

so important," says MSK Instructor in the Leukemia Service Kelly Bolton, who heads the program. "We hope about 100 patients with high-risk forms of CH will participate in our first year."

The MSK investigators who designed MSK-IMPACT, including molecular pathologist Marc Ladanyi and Dr. Berger, believed it was important to look for cancer-related genes in people's normal tissue as well as in their tumors. This would help them determine whether a person's cancer occurred completely by chance or whether inherited factors played a role. The easiest normal tissue to obtain is blood, and the gene mutations linked to CH started to show up as part of MSK-IMPACT testing.

MSK investigators hope to launch clinical trials of treatments that could block the progression from CH to active cancer.

As MSK launches its CH clinic, people who have undergone MSK-IMPACT testing for other cancers and have been found to have high-risk forms of CH in their blood will be contacted by their surgical or medical oncologist and invited to enroll in the program. MSK patients who are treated for low blood counts and found to have CH as part of their blood work will also be seen.

"In the past, CH has been just an incidental finding. When we were worried someone had an undiagnosed blood cancer, we would refer them to the Leukemia Service," Dr. Bolton explains. "Now when we discover patients with high-risk forms of CH, we have a clinic with experts in CH to manage and coordinate their care."

For now, those who enroll in the clinic will have the opportunity to have their blood tested on a regular basis. People who are found to have a blood cancer will be able to start treatment immediately, when the disease is much easier to control.

LOOKING TOWARD FUTURE TREATMENTS

In the future, MSK investigators hope to launch clinical trials of treatments that could block the progression from CH to active cancer. In addition, treatment for solid tumors may be tailored to protect people who already have an increased risk of developing a second cancer. But doctors don't yet know enough about what drives the formation of CH to make any changes to treatment now.

Recent studies suggest that people with CH are at risk for cardiovascular diseases. However, testing for CH is not currently part of screening for them. "It's important for people with CH to follow up with their primary care doctors and make sure they have had the appropriate screenings for cardiovascular diseases," Dr. Bolton says. "We will encourage everyone participating in our CH clinic to do this." ■

SWIM ACROSS AMERICA

Swim Across America (SAA) was established in 1987 by cancer survivor Jeff Keith and his childhood friend Matt Vossler, two former Run Across America participants who transitioned from running to swimming for a cure. Since the first fundraiser was held in Nantucket, Massachusetts, SAA has raised more than $75 million to fund cancer research and clinical trials at world-renowned research institutes and organizations.

One of its major research beneficiaries is MSK, which has been awarded more than $15 million for immunotherapy clinical trials and cutting-edge translational research. SAA funding has played a major role in clinically developing the four US Food and Drug Administration–approved immunotherapy medicines: ipilimumab (Yervoy®), nivolumab (Opdivo®), pembrolizumab (Keytruda®), and atezolizumab (Tecentriq®). Today, more than 5,000 recreational swimmers, masters swimmers, and even kayakers and boaters participate in 15 experiential open-water events and more than 100 pool fundraisers.

James Young, Attending Physician on the Adult Bone Marrow Transplant (BMT) Service and an avid distance swimmer, began swimming in SAA's Long Island Sound Open Water Swim in 2006 and founded Team Transplant in 2009 at the suggestion of a patient, a fellow swimmer who had undergone an allogeneic transplant for acute leukemia. The funds raised by Team Transplant support MSK's Adult BMT program. In July 2018, Team Transplant participated in its tenth consecutive Long Island Sound Open Water Swim and raised close to $19,000. Since 2009, Team Transplant has raised more than $220,000 for much needed support of research efforts that ensure the successful use of transplantation to cure people with leukemia, lymphoma, multiple myeloma, and other cancers of the blood and bone marrow. ■

Team Transplant in 2018, from left: Dick Endris, Jim Young, Jeff Bodenmann, Jeanine Baine, Emily Baine, Nicole Magaldi (with daughter Grace Eddy), and Chris Barbagli; not pictured: Susan McCall

www.swimacrossamerica.org

Q&A
VALKAL BHATT

Along with the dramatic growth of the Adult Bone Marrow Transplant (BMT) Service at Memorial Sloan Kettering over the past five years has come a surge of new medications for these unique patients. It's a wave that clinical pharmacist Valkal Bhatt is happy to have caught.

Dr. Bhatt, who has been on the BMT Service since 2010, "always wanted to be at the front line of managing the care of patients at a time when they're sickest," he says. "Working in a role that MSK has created over the years for pharmacists has enabled me to do that."

About 500 patients received blood or bone marrow transplants at MSK in 2018, the hospital's highest-ever annual total. Accordingly, the number of pharmacists within the BMT Service has grown from four to eight, with still others housed in outpatient and clinic roles.

"The number of medications that our patients take has been increasing just because there are so many more supportive meds for infection prevention and the management of side effects, as well as an explosion of investigational drugs and unique side effects associated with those," Dr. Bhatt explains. "Assessing whether patients are taking those medications appropriately is quite challenging when patients are on 20 or 30 different meds and taking 40 to 50 pills per day."

Arriving at MSK in 2009 as a postgraduate resident in pharmacy oncology, Dr. Bhatt was gratified to work with colleagues to grow and develop the hospital's clinical pharmacy program, which was established only two years prior.

Now the lifelong New Yorker can't see himself living or practicing anywhere else. "Being able to have a premier institution so close by, where I'm able to achieve all my professional goals and define a career path for myself, is so rewarding," he says.

In this interview, Dr. Bhatt highlights his extensive duties, his collaboration with other clinicians, and what he finds most exciting about his role.

What led you into medicine and pharmacology as a career path?

Several of my family members are doctors and pharmacists, and I've always been involved in the healthcare profession. I volunteered in a children's hospital ward when I was young, and while the impact I made was probably minimal, I thought it was so rewarding. As I got older and thought about choosing a career path, I worked part-time in a community pharmacy where I was exposed to medication management from a retail perspective, interacting with patients coming out of the hospital who had questions about their medications. I was able to see the impact a pharmacist can have in patient care, which really drew me toward pharmacy school.

After that, I knew my path was managing people with cancer, and I knew hematologic malignancies and BMT would provide me with the challenge I was looking for and keep me well rounded.

Describe a typical day on the job.

It changes from day to day. On the inpatient service, I round daily with the medical team, and I'm the primary medication manager for those patients. I evaluate all patients admitted on the inpatient service regarding the dosing of the therapies they're on, manage the side effects of treatment, provide adequate supportive care, and manage drug interactions. I also address issues with procuring drugs, such as insurance authorizations, and work with multidisciplinary teams to procure drugs from ancillary teams and investigative drug services to deliver drugs to patients.

In addition, I handle all medication discharge advice and do patient counseling as well. We pharmacists provide an accurate and appropriate list that guides patients on how to take medications, reasonable strategies for organizing their meds, and address any confusion they may have with meds when they leave the hospital. We're also an integral part of the outpatient team, where a pharmacist follows up with patients with complex medication histories, does preadmission counseling, and follows up with complex transplant-related issues that require more frequent management of their therapies.

How much collaboration does your position involve with other clinicians?

It's integral to patient outcomes. Because of the sheer complexity of each BMT patient, it would be a disservice not to collaborate — not only with my pharmacy colleagues who are specialists on the Leukemia or Lymphoma Services to provide a transition to BMT but also with the Infectious Disease Service once patients make it to transplant.

"Being able to have a premier institution so close by, where I'm able to achieve all my professional goals and define a career path for myself, is so rewarding."

Valkal Bhatt
Pharmacist, Adult Bone Marrow Transplant Service

What's the most challenging aspect of your role?

Trying to navigate through changes that occur in drug therapies and the way they're investigated within the institution and the program. There are always new drugs coming out — but how do you develop appropriate guidelines for managing the side effects of those drugs? It's challenging to keep up with change and make sure we're organized so the transition process is seamless and consistent.

How do your interactions with patients influence your efforts?

They're the reason I do this. Helping mitigate the toxicities of treatment and making the transplant process easier for patients from a drug therapy perspective is what makes me happiest. Seeing positive outcomes at the end of it is why I continue to do what I do.

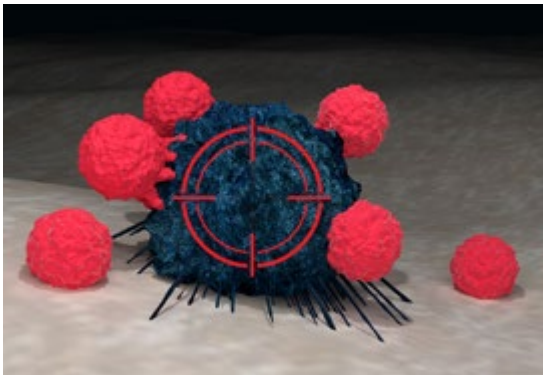
What excites you most about your work?

The ability to be part of the dynamic and continuous positive change that's happening within the service as well as the institution. The whole BMT Service and our multidisciplinary group has one unified goal — to help improve transplant outcomes — and we really work together to achieve that. ■

ADDING LOW-DOSE RADIATION COULD MAKE CAR T THERAPY MORE EFFECTIVE, STUDY FINDS

By Matthew Tontonoz

A study by researchers at Memorial Sloan Kettering done in mice shows that radiation therapy can improve how chimeric antigen receptor (CAR) T cell therapy works against solid tumors.



T cells (red) can be genetically modified to recognize cancer cells (blue) with certain characteristics. Radiation therapy (represented by crosshairs) may help these engineered immune cells kill more tumor cells.

For people with certain leukemias and lymphomas, an immunotherapy with CAR T cells has proven to be potentially lifesaving. The US Food and Drug Administration approved two such therapies in 2017.

The approach's success in treating these cancers stems, in part, from the presence of a clear target: a molecule on the surface of blood cancer cells called CD19. CAR T cells outfitted with a protein that latches on to CD19 can easily find and destroy these cancer cells.

CD19 flags nearly all blood cancer cells, but such a prime target is hard to come by in other cancers. This makes it challenging to extend the benefits of CAR therapy to other cancer types, including solid tumors, like lung cancer, breast cancer, and pancreatic cancer.

One way to address this problem, new research from MSK suggests, is by combining CAR therapy with radiation therapy.

"We found that radiation made it easier for CAR T cells to kill tumor cells, including tumor cells that did not express the CAR target and would otherwise escape from the CAR therapy," says Michel Sadelain, Director of the Center for Cell Engineering at MSK and the corresponding author on a paper published October 25, 2018, in *Molecular Therapy*. "We made this discovery in a mouse model of pancreatic cancer, but the approach is applicable to any cancer in principle."

NOT WHAT THEY EXPECTED FROM ADDING RADIATION

Pancreatic ductal adenocarcinoma (PDAC) is a deadly cancer that is currently hard to treat with anything other than surgery. CAR therapy has so far not been effective. In part, that's because the tumor cells are not all alike with respect to potential CAR targets. Although some cells have markers that could be targets for CARs, not all cells have them, making it difficult to design a CAR that would work against every cancer cell in the tumor.

One marker that is found intermittently in pancreatic cancer is called sialyl Lewis-A (sLe^A). The researchers wondered if radiation might spur more of the PDAC cells to express, or make, this marker.

They gave mice low-dose radiation before administering the sLe^A-specific CARs. They found that the combination of radiation and CARs did indeed increase the amount of tumor that was destroyed but not in the way they had initially hypothesized. That is, the number of cells making sLe^A — the CAR target — did not change.

"That's when we knew that some other mechanism of killing must be involved," Dr. Sadelain says.

ON THE TRAIL OF A NEW CAR T ROLE

Carl DeSelm, a physician-scientist working in Dr. Sadelain's laboratory, analyzed what genes were turned on in the cells before and after low-dose radiation. He used a technique called RNAseq, which measures messenger RNA transcribed from genes. He found that radiation triggered the cells to turn on genes related to a kind of programmed cell death. The process is initiated by a protein called TRAIL (short for tumor necrosis factor–related apoptosis-inducing ligand). When TRAIL is present in the area around cells that have these genes turned on, those cells are cued to self-destruct.

Next Dr. DeSelm wanted to find out if CAR T cells produce TRAIL, so he analyzed RNA and protein produced by these cells in the presence and absence of a tumor. He found that TRAIL production goes way up when the CAR T cells bind to the sLe^A target.

And here's where it gets really interesting. The combination of radiation and CARs resulted in the death of pancreatic tumor cells that have the sLe^A target as well as those that do not.

A SINGLE HUMAN CASE: A PERSON WITH LYMPHOMA

Researchers won't know for sure whether the same holds true in people with cancer until they conduct a clinical trial, which is currently being planned. But one known case report gives them hope. A person with lymphoma who was to receive CD19 CAR therapy had noncurative local radiation to his leg first, to relieve pain resulting from the disease.

Weeks later, after initially subsiding, the disease rebounded in various spots around his body. But it did not grow in the area that was irradiated. This result suggests — although it does not prove — that the radiation sensitized the tumor cells in his leg to TRAIL-mediated CAR T killing.

"Radiation therapy is currently used at some point in the treatment of about half of people with cancer that has spread, and for others it is commonly employed to improve tumor control in nearly all types of cancer," says Dr. DeSelm, who is now an assistant professor of radiation oncology at Washington University in St. Louis. "Our hope is that CAR therapy might provide people with an added benefit when integrated with these standard radiation procedures."

MSK medical oncologist Lia Palomba and radiation oncologist Joachim Yahalom, also authors on the paper, will be leading a clinical trial to test this approach. ■

This study was supported by the MSK Molecular Cytology Core Facility, which is funded by an MSK Core Grant (P30 CA008748 S) and a grant from the National Institutes of Health (U54 OD020355-0); the Integrated Genomics Operation Core, which is funded by a National Cancer Institute Cancer Center Support Grant (P3014CA08748); and a Geoffrey Beene Research Foundation Shared Resources Grant.

The study's authors declare no potential conflicts of interest. A patent application has been submitted by MSK based in part on the results reported in this study.

STUDY SHOWS THAT 9/11 WORKERS ARE AT A HIGHER RISK FOR A PRECURSOR TO MULTIPLE MYELOMA

By Jim Stallard

Ola Landgren, Chief of the Myeloma Service, says that the study supports the idea that multiple myeloma can be triggered by environmental factors.

Research shows that firefighters who worked at the World Trade Center (WTC) scene are nearly twice as likely to have a precursor condition that could lead to multiple myeloma, the second most common blood cancer in adults. The study provides more evidence supporting the idea that multiple myeloma can be triggered by environmental factors.

Ever since the September 11, 2001 attack, there have been mounting concerns that rescue and recovery workers at the WTC site were exposed to hazardous materials that could cause long-term damage to their health. Now, research led by Memorial Sloan Kettering shows that firefighters present at Ground Zero in the immediate aftermath may be at an increased risk for developing a blood cancer called multiple myeloma.

The study, published in *JAMA Oncology,* reveals that firefighters at the scene were nearly twice as likely to have a multiple myeloma precursor condition called monoclonal gammopathy of undetermined significance (MGUS). This is the first comprehensive study showing that WTC first responders are at higher risk for MGUS. In addition, the researchers found that the firefighters may be at a higher risk for developing multiple myeloma at an earlier age, as well as a more lethal form of the disease.

"Although MGUS will not necessarily lead to multiple myeloma, it is always present as a preliminary stage before someone develops the disease," says Ola Landgren, Chief of MSK's Myeloma Service, who led the study. "It can serve as an early warning."

In 2015, Dr. Landgren published research showing that exposure to Agent Orange, an herbicide that was widely used during the Vietnam War, also increased the risk of having MGUS and multiple myeloma. The new study provides more evidence supporting the idea that multiple myeloma can be triggered by environmental factors.

Rescue and recovery workers may have been exposed to known carcinogens in the dust from the collapsed buildings and from diesel smoke emitted by heavy equipment used in the search. The findings suggest that these first responders should consider being checked for MGUS. The condition, which is marked by elevated levels of a protein called M protein, can be detected with a simple blood test.

"The clinical guidelines for multiple myeloma don't currently address being tested for MGUS," Dr. Landgren says. "But for people who spent significant amounts of time around the recovery site, it is reasonable for them to speak with their primary care doctor about being checked for this precursor condition. This could apply even to people who didn't work at the site but lived or worked nearby at the time."

Most people with MGUS remain well for many years without developing multiple myeloma. But Dr. Landgren says that anyone who learns they have MGUS should have their protein levels monitored going forward through annual blood tests to watch for multiple myeloma. This monitoring can typically be done by a primary care doctor. If multiple myeloma is suspected, further diagnostic tests, including imaging, blood, urine, and bone marrow tests, would be recommended.

MULTIPLE MYELOMA: A SLOW-MOVING BUT INCURABLE CANCER

Multiple myeloma, the second most common blood cancer among adults, arises from a type of white blood cell called a plasma cell. The disease is usually treated with chemotherapy, immune-modifying drugs or other medications, or stem cell transplantation. It can be held at bay for many years, but there is no cure. When it relapses, it becomes resistant to further treatment.

Although there are currently no drugs approved to treat MGUS, close monitoring could still benefit someone who eventually develops multiple myeloma. A 2015 study led by Dr. Landgren showed that people with MGUS who develop multiple myeloma during clinical monitoring have better overall survival and fewer complications than those who never received an MGUS diagnosis. This is likely because treatment of multiple myeloma begins sooner, which makes it more effective.

INCREASED RISK AND EARLIER ONSET

In the study, the researchers screened blood samples from 781 WTC-exposed male firefighters. As a comparison population, they used published data on MGUS from a group of 7,612 men in Minnesota.

The firefighters had enrolled in the WTC Health Program to receive physical and mental health services and consented to have blood samples analyzed for research. The samples were tested at MSK.

The researchers found that the prevalence of MGUS in this group was approximately twice as high as in the comparison group. The rate in the study group was 7.73 per 100 people compared with 4.34 in the comparison group.

A second part of the study looked at all firefighters at the WTC site who had developed multiple myeloma between September 11, 2001, and July 1, 2017. The median age of onset for the disease was 57 years — about 15 years earlier than the general population. The firefighters were also more likely to have aggressive types of the disease compared with the overall myeloma population.

"It's possible that specific environmental factors can cause specific subtypes of myeloma, including those that are more or less aggressive," Dr. Landgren says. ■

This work was supported by the V Foundation for Cancer Research, the Byrne Fund for the benefit of Memorial Sloan Kettering, the Memorial Sloan Kettering Cancer Center Core Grant from the National Cancer Institute (P30 CA008748), the Albert Einstein Cancer Center (P30 CA013330), and the National Institute for Occupational Safety and Health (grant 1 U01 OH011475 and contracts 200-2011-39383, 200-2011-39378, 200-2017-93326, and 200-2017-93426).

BMT THRIVERS

On October 2, more than 700 people joined the 23rd annual celebration for blood and marrow transplant thrivers.

Two hundred MSK patients came from half a dozen states, bringing along hundreds of family, friends, donors, and caregivers to celebrate with them. They were joined by the doctors, nurses, and other staff from the Bone Marrow Transplant (BMT) Service who care for people during their complex and grueling return to health after a transplant.

As always, the event featured incredible reunions. Geri Hotard, a BMT recipient from Connecticut, brought the crowd to their feet — many of them in tears — when she introduced Michael Meister, whose bone marrow donation helped save her life. Mr. Meister traveled to the event from his home in Germany, and now these former strangers share a lifelong bond.

BMT Service Chief Sergio Giralt remarked that just as the celebration grows every year, so too does the number of BMT recipients cared for by MSK. In 2018, for the first time, MSK doctors performed more than 500 adult transplants. He also promised that MSK will continue its efforts to improve access so people can get the transplants they need. He noted that because of the MSK Cancer Alliance, many more people are receiving lifesaving transplants. ■

Donor Michael Meister and MSK patient Geri Hotard

Parastoo Dahi

From left: Erika George, Tanya Gelfand, Sergio Giralt, Chelsea Brooklyn, and Ally Manley

STEVEN HORWITZ'S RESEARCH INTO RARE LYMPHOMA FUELS A MAJOR TREATMENT BREAKTHROUGH

Steven Horwitz

Progress is often slow and incremental in medicine, but sometimes new data can prompt change amazingly quickly. Such is the case with a new treatment approach to a rare form of lymphoma that Steven Horwitz has studied since joining Memorial Sloan Kettering in 2001.

In the span of three months in late 2018, a worldwide clinical trial led by Dr. Horwitz and colleagues produced such stunning results that it set off a domino effect, with a rapid approval by the US Food and Drug Administration and an immediate change to treatment guidelines for certain patients with newly diagnosed peripheral T cell lymphoma (PTCL).

The phase III study, known as the ECHELON-2 trial, showed progression-free survival times more than doubled and overall survival improved by more than 30 percent among patients receiving the targeted drug brentuximab vedotin (Adcetris®) along with chemotherapy for PTCL compared to chemotherapy alone.

The FDA took only 11 days to review the data before approving the drug for PTCL in late November. And by early December, Dr. Horwitz had presented the data to great acclaim at the prestigious American Society of Hematology conference with simultaneous publication in *The Lancet*.

The series of events marked a milestone for Dr. Horwitz, Attending Physician in the Lymphoma Service, who has focused his research on less-common types of lymphoma, including T cell and cutaneous (skin) lymphomas. While he and others had identified and developed new drugs and approaches for patients with relapsed PTCL, until this study adding brentuximab vedotin to a chemotherapy backbone, little had changed in the upfront treatments for PTCL in two decades.

"Certainly, it's the first study in T cell lymphoma to show an overall survival benefit over any kind of control or standard treatment, so it's a huge advance for us and our patients," he explains. "As a rare disease, T cell lymphoma is not a public health problem, but for the people who have it, the lack of progress has been frustrating and scary. This provides an immediate better treatment option for many, but we also hope it's a paradigm we can build on with future drugs for other diseases."

FILLING A "BIG UNMET NEED"

Brentuximab vedotin is a monoclonal antibody that targets a protein called CD30 found on some cancer cells. Dr. Horwitz and colleagues wanted to test the drug — already FDA-approved for relapsed CD30-expressing lymphomas, such as Hodgkin lymphoma and a PTCL subtype called anaplastic large cell lymphoma — in patients whose PTCL cells expressed lower or variable CD30 levels.

Until this point, standard treatment for PTCL often involved a chemotherapy regimen known as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone). The ECHELON-2 trial — following on the heels of an encouraging MSK phase I study for safety — included more than 450 patients in 17 countries. It split patients into two groups, comparing the standard CHOP regimen to a combination of brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone. Vincristine was omitted because of its specific side effects that might add to the toxicity of brentuximab vedotin.

"Historically, we treat PTCL with curative intent, most often with a combination of chemotherapy drugs, often incorporating a bone marrow or stem cell transplant," Dr. Horwitz explains. "Even with that maximal chemotherapy approach, the majority of patients weren't cured. Relapse too frequently leads to shortened survival, so there was a big unmet need for other therapies to improve our initial treatment."

CRUCIAL GLOBAL COLLABORATION

Key among ripple effects from the newly published data was an immediate change in practice guidelines for PTCL across the field among CD30-positive patients. "With the overall survival benefit, I think it will be a standard or very commonly used regimen for a lot of these patients," Dr. Horwitz notes.

Eligible MSK patients, however, have benefited from this advance since the beginning of the ECHELON-2 trial more than five years ago. Dr. Horwitz estimates that between 20 to 30 PTCL patients will be treated with this approach at MSK each year.

Brentuximab vedotin in combination with chemotherapy "works really well," he says. "Almost everyone has a response. We want to include all patients who would benefit."

He credits extensive collaboration among MSK and more than 100 centers on four continents for the breakthrough. Perhaps one of MSK's particular strengths compared to others, he says, is our ability to truly subspecialize in rare diseases. Individuals here can maintain a focus and develop an expertise, allowing us to answer important questions even on rare or ultrarare subtypes of lymphoma.

However, progress is often best made by working together. "At least for this rare disease, PTCL, we've had continual collaboration on all of our studies with colleagues both nationally and internationally," Dr. Horwitz explains. "I think it's one of the rewarding aspects of this field that people really do work together for the benefit of our patients. As a large center, we have been fortunate enough to have a major role in designing and conducting these studies, but the field mostly pulls together and the successes are truly shared."

BUILDING ON SUCCESS

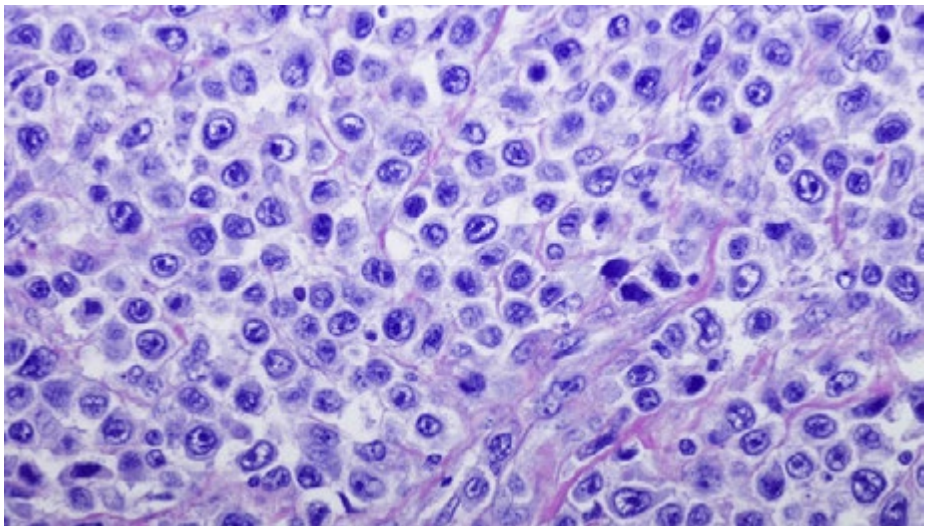
Dr. Horwitz hopes to use these results as a blueprint for future studies that are similarly impactful, potentially changing more treatment paradigms. A number of additional MSK studies are focusing on CD30-positive patients, which Dr. Horwitz says is "a relatively easily identifiable biomarker to use to select those who could benefit."

For example, MSK collaborated with Stanford University and others to examine the drug's effects in cutaneous T cell lymphoma. Published results led to its FDA approval as a single agent for patients whose disease has relapsed.

"Beyond CD30, this research suggests that as we develop active drugs and are then critically able to identify which tumors are most vulnerable and which patients will most likely benefit, we can make meaningful impacts with this simple approach of adding to combination therapies," Dr. Horwitz says. "Identifying patients most likely to benefit is rarely simple or straightforward, but it is a major effort of ours and is shaping how we design new studies going forward." ■

RESEARCHERS DISCOVER A NEW STRATEGY FOR FOILING DRUG RESISTANCE IN AGGRESSIVE LYMPHOMA

By Jim Stallard



Diffuse large B cell lymphoma is the most common type of non-Hodgkin lymphoma. A combination drug strategy holds potential for slowing or stopping this fast-growing blood cancer.

A promising target in the treatment of diffuse large B cell lymphoma (DLBCL) is a protein called BCL2. Drugs that inhibit this protein have been disappointing so far. Researchers have now discovered why DLBCL often proves resistant to this treatment. They have shown that a combination drug strategy could be effective at treating this aggressive form of non-Hodgkin lymphoma.

DLBCL, an aggressive cancer of the white blood cells, is the most common form of non-Hodgkin lymphoma. Researchers looking to slow or reverse this cancer have zeroed in on one particular target, a protein called BCL2. Excessive amounts of BCL2 can help lymphoma cells survive.

In 2016, the US Food and Drug Administration approved a BCL2-targeted drug, venetoclax (Venclexta®), for chronic lymphocytic leukemia. It and similar drugs are being tested in other BCL2-dependent blood cancers. Researchers have had especially high hopes for using BCL2 inhibitors to treat people with different types of lymphoma. But BCL2-targeted drugs have been disappointing in people with DLBCL. In most cases, the tumors resist the treatment.

Now a team led by Anas Younes, Chief of Memorial Sloan Kettering's Lymphoma Service, has discovered why DLBCL resists BCL2 inhibitors. The researchers have also developed a strategy for overcoming this resistance, and it appears to be effective in cell lines in the lab and mice. The approach involves combining BCL2 inhibitors with a second drug. The pairing will be tested in people with DLBCL within the next year.

The findings were reported in the *Proceedings of the National Academy of Sciences*.

BLOCKING TWO DISEASE PATHWAYS

The researchers discovered that in DLBCL tumors, BCL2 has a backup actor — a protein called MCL1. Blocking BCL2 alone is not enough to kill most tumors because MCL1 can pick up the slack. The team showed that in human DLBCL cells and mouse models for the disease, blocking both proteins with a combination of two drugs effectively killed the tumors.

Intriguingly, the team also found an alternate way to make DLBCL cells sensitive to BCL2 inhibitors. They studied a wide range of lymphoma cells treated with BCL2 drugs and looked for the few that actually responded. They identified two types of DLBCL cells that are sensitive to treatment with a BCL2 inhibitor alone. These cells had high levels of a protein called NOXA, a natural inhibitor of MCL1.

The researchers speculated that spurring higher production of NOXA in tumors might be as effective as trying to inhibit MCL1 directly. One way to boost NOXA production is through a class of drugs called HDAC inhibitors. In further studies with cell lines and mouse models, the research team showed that HDAC inhibitors made DLBCL cells vulnerable to the effects of BCL2 inhibitors.

"This suggests that combining BCL2 inhibitors with either MCL1 inhibitors or HDAC inhibitors could also be effective in people with DLBCL," Dr. Younes says. "We don't know which approach will work best or which type of inhibitor will be less toxic to people. It's clearly better to have more than one treatment option."

BROAD THERAPEUTIC POTENTIAL

Dr. Younes explains that blocking HDACs may provide added benefits. HDAC inhibitors not only neutralize MCL1, they also tamp down the effects of another protein called MYC, which promotes lymphoma and other cancers. In fact, people whose DLBCL has genetic changes in both of these proteins — known as double-hit lymphoma — have the worst prognosis. So a drug combination targeting HDAC and BCL2 could theoretically offer a better outcome.

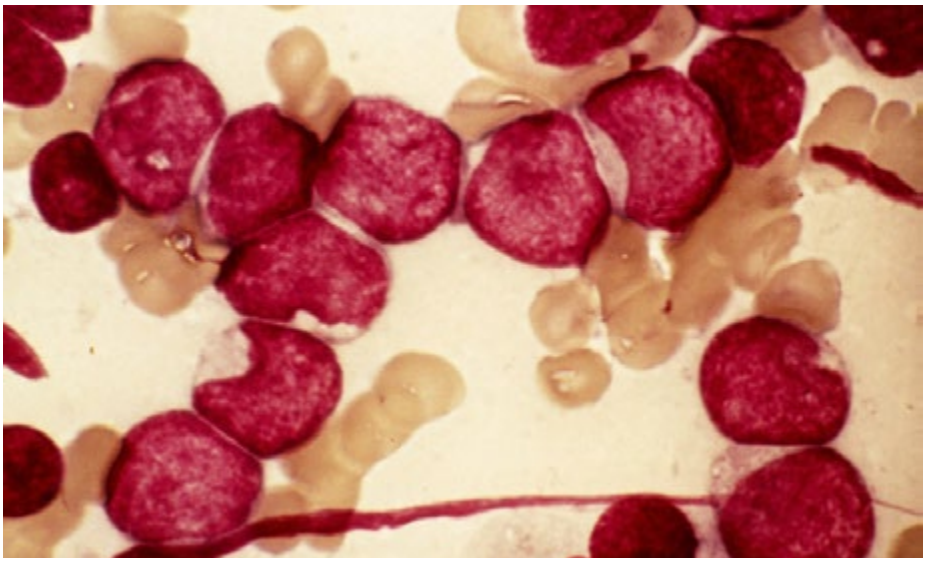
Dr. Younes says that the clinical trial will combine a BCL2 inhibitor with an HDAC inhibitor in people whose double-hit DLBCL has returned after initial treatment. He expects the phase I/II trial to begin at MSK sometime in 2019.

"We're very excited about these findings and the potential of the combination approach," he says. ■

This work was supported by a National Institutes of Health grant for MSK's Lymphoma SPORE (T3151) , a National Cancer Institute Cancer Center Support Grant (P30 CA008748), Cycle for Survival, and the Marie-Josée and Henry R. Kravis Center for Molecular Oncology. The study was funded in part by a research grant from Servier, which provided a BCL2 inhibitor used in the experiments. Dr. Younes received research funding for clinical trials from both Servier and Novartis.

FINDINGS FROM TWO PATIENTS SHED LIGHT ON DRUG RESISTANCE IN AML

By Julie Grisham



Acute myeloid leukemia starts in the blood-forming cells of the bone marrow.
Source: Pr. J. Bernard/CNRI/Science Source

Drug resistance is when a tumor stops responding to a targeted therapy. It is a serious problem in cancer treatment. Now, a multidisciplinary team has discovered a previously unknown mechanism of resistance to a new leukemia drug.

In 2017, the US Food and Drug Administration approved enasidenib (Idhifa®) for the treatment of acute myeloid leukemia (AML). Enasidenib works differently than most cancer drugs. Rather than killing leukemia cells, it turns them into normal blood cells. Memorial Sloan Kettering hematologic oncologist Eytan Stein led the pivotal clinical trial that resulted in the drug's approval.

Now, a collaborative team of researchers has reported that people who take enasidenib can develop resistance to it — and in a way never seen before. The findings were reported in *Nature*.

"Everyone who studies precision medicine spends a lot of time thinking about why some people respond to certain drugs and why some stop responding or never respond at all," says physician-scientist Ross Levine, who was one of the paper's senior authors, along with Dr. Stein. "MSK has been one of the leaders in figuring this out."

The discovery was made by a team of doctors, laboratory researchers, and pharmaceutical company scientists. They used cells from people who were being treated with enasidenib to uncover why the drug sometimes stops working.

TARGETING A MUTATION FOUND IN SEVERAL CANCER TYPES

Enasidenib is approved for people with AML that is driven by a mutation in a gene called *IDH2*. About 15 percent of people with AML have this mutation. *IDH2* mutations and mutations in the related gene *IDH1* are found in other types of leukemia as well as myelodysplastic syndromes, glioblastoma, and bile duct cancer.

The proteins made from mutated IDH genes can drive cells to become cancerous. MSK President and CEO Craig Thompson conducted much of the fundamental research on IDH mutations and their relationship to cancer. He is one of the co-authors of the *Nature* paper.

Researchers had previously shown that only one of the two copies of the *IDH2* gene needs to be mutated to drive cancer. The other one is usually normal. In the *Nature* paper, the investigators report that when cells developed resistance to enasidenib, the additional mutations that allowed the cells to resist the drug occurred on the normal copy of *IDH2*.

This stands in contrast to how resistance develops against most targeted cancer therapies. In those cases, an already mutated gene develops an additional mutation that allows the cancer cell to fend off the drug's effects. "The finding about *IDH2* suggests that genetic resistance is more complicated than we thought," says Dr. Levine, who is a member of MSK's Human Oncology and Pathogenesis Program (HOPP).

Just two patients were in the study, but the investigators learned a great deal. Experiments with laboratory models allowed them to study how the mutations work. The findings suggest that some people may develop resistance to IDH inhibitors due to a mutation on the same copy of the gene that carries the cancer-causing mutation.

Dr. Levine says that this prediction was confirmed when the researchers identified a third patient being treated with a similar drug that targets a mutation in *IDH1*. The IDH inhibitor stopped working in this person when a resistance mutation appeared on the copy of the *IDH1* gene with the cancer-causing mutation. This suggests that the process may be universal to all IDH-blocking drugs. "It's a small number of people, but we're quite confident that we'll see this same mechanism in others moving forward," he adds.

Targeting IDH mutations is a growing area of cancer drug development. Earlier this month, Dr. Stein was a co-first author of a paper published in the *New England Journal of Medicine* that looked at another drug that targets the *IDH1* mutation in people with AML. The multicenter phase I trial reported data on 125 people whose cancer had stopped responding to other treatments. The researchers found that of those treated with the drug, ivosidenib (Tibsovo®), almost 42 percent responded. Nearly 22 percent had a complete remission, meaning that their cancer was no longer detectable. The overall survival was longer than what would be expected in people with this stage of AML and severe side effects were rare. The researchers plan to continue studying the drug in larger placebo-controlled trials.

"Now that we know resistance to enasidenib can develop, we can start to monitor people for it."

Andrew Intlekofer
Physician-Scientist

A NEW BIOMARKER FOR DRUG RESISTANCE

After the people in the study developed resistance, their tumors started growing again. Doctors were able to switch them to other drugs that worked in a different way, however, so they were not affected by the additional mutation. There are a number of other treatment options for people with AML. These include both FDA-approved therapies and experimental drugs being tested in clinical trials. Many people with AML ultimately receive stem cell or bone marrow transplants, which offer the opportunity for a cure. However, many people are not able to undergo transplants, which makes developing new drugs an important focus.

"Now that we know resistance to enasidenib can develop, we can start to monitor people for it by conducting blood tests," says first author Andrew Intlekofer, who is also a physician-scientist in HOPP. "Over the course of therapy, we can use the protein as a biomarker for the formation of resistance. Then we'll know we need to offer a different treatment."

FAR-REACHING IMPLICATIONS FOR OTHER CANCERS

Understanding how resistance to enasidenib develops could lead to the development of additional drugs. Although, Dr. Intlekofer adds, more research is needed before new drugs can be identified. He also notes that the new discoveries about enasidenib could apply to other drugs that work in a similar way. Treatment of other cancers that are characterized by *IDH1* and *IDH2* mutations could be affected as well.

Dr. Levine highlights the importance of collaboration when conducting this kind of research. Working closely with scientists from Agios, the company that makes enasidenib, was of particular importance, he says. "To do this kind of work, it requires a great team. Everyone who worked on this study made important contributions. This work was one of the most satisfying research experiences I've ever had." ■

The Nature *study was funded by National Cancer Institute grants (K08 CA201483, K08 CA181507, R01 CA168802-02, R35 CA197594-01A1, U54 OD020355, and P30 CA008748); the Leukemia and Lymphoma Society; the Burroughs Wellcome Fund; the Susan and Peter Solomon Divisional Genomics Program; the Steven A. Greenberg Fund; the Translational and Integrative Medicine Research Fund; the American Association for Cancer Research; the American Society of Hematology/Robert Wood Johnson Foundation; Cycle for Survival; and the Marie-Josée and Henry R. Kravis Center for Molecular Oncology. The* NEJM *study was funded by Agios, which also makes ivosidenib.*

Tracy Seguljic with her teenage son

A CANCER PARTNERSHIP HELPS SAVE A LOCAL WOMAN'S LIFE

By Steve Coates

For months, Tracy Seguljic hadn't been feeling well. She had recently lost her husband to glioblastoma, an aggressive form of brain cancer, and believed she was suffering from exhaustion brought on by her grief and the months spent caring for her husband and two teenage sons.

After experiencing shortness of breath, Seguljic went to the emergency department at MidState Medical Center, where a bone biopsy confirmed that she had acute myeloid leukemia (AML).

"I was told to prepare for a month in the hospital. But at no point did I ever think I was going to die," Seguljic says.

From the emergency department, oncologist Susan Alsamarai quickly began to develop a strategy for Seguljic's care, which included an aggressive form of chemotherapy.

"We needed to get things started quickly. We worked with pathology to get the results so we would know what the right course of treatment should be. We needed to know what leukemia she had and what mutations she might have," says Dr. Alsamarai.

Seguljic had a mutation known as SLIT3, which makes the cancer even more aggressive. Luckily for Seguljic, her treatment worked, and within two months her cancer went into remission. The next step was for Seguljic to have a bone marrow transplant. Thanks to the Hartford HealthCare Cancer Institute's membership in the Memorial Sloan Kettering Cancer Alliance, Seguljic's transplant was seamlessly coordinated by MidState and the world-renowned specialists at MSK.

"It was very smooth getting her [to MSK in New York City] and expediting the transplant. This was 2015, and we had just begun our relationship with MSK. It was a good prototype of how we carry out this relationship," says Dr. Alsamarai.

Seguljic's transplant, made possible through a marrow donation from her sister, was a success. Four years into the partnership with MSK, the Hartford HealthCare Cancer Institute now employs a bone marrow coordinator who facilitates transplants like Seguljic's and follow-up care.

Seguljic credits the quick thinking by the team at MidState and the expertise of MSK in helping her beat leukemia. But it's her faith that has guided her emotionally through some pretty dark days, she says.

"This is just a bump in the road. You lean on God and don't sweat the little things," she says. ■

FDA APPROVES IVOSIDENIB, A TARGETED DRUG, FOR ACUTE MYELOID LEUKEMIA

By Julie Grisham

Hematologic oncologist Eytan Stein with nurse practitioner Bernadette Cuello

Ivosidenib (Tibsovo®) is the first drug in a class called IDH1 inhibitors to receive approval from the US Food and Drug Administration. It works by targeting a defect in cancer cells.

Ivosidenib has been approved for the treatment of certain people with acute myeloid leukemia (AML) that has stopped responding to other therapies. Memorial Sloan Kettering hematologic oncologist Eytan Stein was a co-leader of the study that led to the drug's approval. The results of the trial were published last month in the *New England Journal of Medicine* (*NEJM*), and the drug was approved on July 20, 2018.

Ivosidenib is the first drug in a class called *IDH1* inhibitors to receive FDA approval. It works in a similar way as enasidenib (Idhifa®), a drug approved in 2017 to treat AML that's driven by a mutation in a related gene, *IDH2*. Both drugs represent a "new approach to treating cancer," says Dr. Stein.

"Instead of killing cancer cells, like other leukemia drugs, it reprograms them and transforms them into normal, healthy, functioning cells," he says.

About 10 percent of people with AML have mutations in the *IDH1* gene, and another 15 percent have *IDH2* mutations. These mutations are also found in other types of leukemia as well as myelodysplastic syndromes, glioblastoma, and bile duct cancer. Targeting these mutations is a growing area of cancer drug development.

MSK President and CEO Craig Thompson led the basic science research that explains how *IDH1* mutations drive AML, in collaboration with MSK physician-scientists Ross Levine and Omar Abdel-Wahab. The Peter and Susan Solomon Family Foundation supported that research, which was first reported in 2010. The investigators found that the mutations produce a cancer-causing enzyme called hydroxyglutarate (2HG). This enzyme stops the development of the blood cells called myeloid cells when they are in an immature form, which leads to leukemia.

Ivosidenib brings down the level of 2HG, so the blood cells can begin to develop normally again.

The *NEJM* study was a multicenter phase I trial that reported data on 125 people whose cancer had stopped responding to other treatments. The researchers found that of those treated with ivosidenib, almost 42 percent responded. Nearly 22 percent had a complete remission, meaning that their cancer was no longer detectable. The overall survival was longer than what would be expected for people with this stage of AML, and severe side effects were rare.

MSK Leukemia Service Chief Martin Tallman also participated in the study. ■

Leukemia Service Chief Martin Tallman is leading clinical trials for new leukemia drugs.

Ivosidenib and enasidenib are both made by Agios Pharmaceuticals.

JOB DESCRIPTION: SOLVES PROBLEMS, PUTS OUT FIRES

Anne Marie Gonzales-Dadiz deftly oversees clinical research in the Division of Hematologic Malignancies.

Some of Anne Marie Gonzales-Dadiz's fondest early memories center around her beloved grandfathers, both of whom died from cancer. So an opportunity to work in clinical research at Memorial Sloan Kettering "hit close to home," says the Philippines native, who ruled out medical school in favor of taking on a research role.

Arriving at MSK in 2005, Ms. Gonzales-Dadiz has spent the past five years overseeing clinical trials for the Division of Hematologic Malignancies as Research Program Manager. While her job may be somewhat behind the scenes, it's also a crucial cog in the wheel: Staffing and running the more than 200 research projects currently underway in the division is no mean feat.

Ms. Gonzales-Dadiz is one of ten such managers at MSK and one of four in the Department of Medicine.

"I don't ever feel I don't get the credit I deserve, whether from individual doctors I work with or within the division," Ms. Gonzales-Dadiz says. "Even within clinical research and the leadership above me, we're constantly told there's a reason there's so many of us — it's because we play a vital role in making sure things get done."

FACE TIME FACILITATES HER ROLE

If you ask Ms. Gonzales-Dadiz what a typical day on the job involves, her quick answer is: "Endless meetings." But perhaps that's unavoidable, since those meetings encompass researchers and clinicians investigating therapies spanning leukemia, lymphoma, multiple myeloma, bone marrow transplant, benign hematology, and cellular therapeutics.

All of that face time, however, helps ensure that clinical trials "are running as smoothly as possible," she explains. "Do the teams have adequate staff? Is it appropriate to participate in the trial from an operational standpoint? Is this something we can feasibly do or manage?"

Along with answering those pressing questions, Ms. Gonzales-Dadiz is tasked with improving efficiency through such means as centralizing the CVs and medical licenses of all research investigators at MSK, as well helping improve compliance with serious adverse events reporting.

"Because there's a better understanding of solid tumors, a lot of processes in place are more solid tumorcentric, but what works for solid tumors doesn't necessarily work for liquid tumors. I make sure our needs are represented in other working groups and process improvement initiatives."

Anne Marie Gonzales-Dadiz
Research Program Manager,
Division of Hematologic Malignancies

She also serves as a liaison to MSK's clinical research leadership with a particular eye toward representing the specific needs of hematological malignancies.

"Because there's a better understanding of solid tumors, a lot of processes in place are more solid tumorcentric," she says. "But what works for solid tumors doesn't necessarily work for liquid tumors. I make sure our needs are represented in other working groups and process improvement initiatives."

PROUD MOMENTS

With more than a decade under her belt at MSK, Ms. Gonzales-Dadiz isn't short on memorable moments. The research study she's most proud of being part of involved seven centers completing a retrospective analysis of patients with Hodgkin lymphoma who later developed breast cancer. Ms. Gonzales-Dadiz, then a Research Study Assistant, developed the database that compiled records on 1,000 patients.

"I was able to see the data come to fruition and be published," she recalls proudly. "Even though I left to join the Adult BMT Service, my input was still solicited and valued by the time it became a manuscript."

Also gratifying to Ms. Gonzales-Dadiz is witnessing some of the research staff members she mentored many years ago continue to progress in their MSK careers.

"I'm seeing a lot of my very first direct reports grow into managers and dedicate themselves to the work I've been dedicated to," she says. "They're also devoted to the center and to the groups they manage."

SHARED MISSION

In Ms. Gonzales-Dadiz's role, perhaps it's inevitable that constant collaboration with research staff unearths problems within a clinical trial process that Ms. Gonzales-Dadiz must then fix. "I definitely want to know if things aren't working," she notes. "My colleagues appreciate this, and vice versa."

Constantly putting out fires can be tedious, Ms. Gonzales-Dadiz acknowledges, and yet, she says, "It's an expected part of my role."

In her eyes, the most difficult aspect of her position is implementing new initiatives, since MSK's size alone translates into unavoidable delays to ensure that all of the key players are all apprised of new developments and decisions are vetted accordingly.

"We're all here for the same mission," Ms. Gonzales-Dadiz explains. "And that definitely helps if there's a tense situation. At the end of the day, because we all believe in the same thing, it makes it easier to put our differences aside and ask, 'How can we make things happen successfully?'

"Every day here can be something different, and something interesting always pops up," she adds. "Whether it's good or bad, I'll take it." ■

TEAMWORK IS PARAMOUNT TO ADVANCES IN MYELOMA TREATMENTS AND TESTING

When Ola Landgren was recruited to become Chief of the Myeloma Service in early 2014, he aimed to put Memorial Sloan Kettering on the map as a worldwide leader in myeloma treatment and research as well as novel myeloma drug development. But that lofty goal required an equal push to build a comprehensive, collaborative team that could advance MSK's clinical trial research on many disease fronts.

Less than five years later, the efforts of Dr. Landgren and his team have already paid off in stunning ways. The Myeloma Service has tripled in size, including both patient volume and team members, while enrolling more than ten times more patients on clinical trials and attracting far higher levels of grant and contract funding than it once did.

Myeloma Service Chief Ola Landgren with clinical trials nurse Donna Mastey (left) and clinical research manager Natasha Jafri (right)

Among the 12 research staff members Dr. Landgren deems integral to the service's research progress are Donna Mastey, one of four clinical research nurses in the service, and Natasha Jafri, a clinical research manager. Together, the trio represent various perspectives — clinical, administrative, data tracking, and otherwise — that comprise MSK's successful myeloma clinical trials program. "Welcome to the MSK myeloma family," Dr. Landgren says.

"We've really focused on the development of new therapies and different and improved strategies for treating patients," he says. "We use all of our clinical trials as one of the main drivers for the development of the service. Within just a few years we've tripled the size of our service, thanks to the work the whole team is doing, whether in clinical, data, administration, or other roles. It really is a group effort."

People with myeloma across the globe are reaping the benefits of MSK's groundbreaking clinical trial advances, often made in concert with other top-tier centers. With nearly a dozen new myeloma drug therapies approved since 2000, patients diagnosed in 2019 can expect an average survival of ten to 20 years — up from less than five years two decades ago.

"We still have gaps to fill," Dr. Landgren explains. "We don't yet have a curative treatment — it's a chronic disease management situation, and unfortunately, patients who develop recurrent disease eventually become nonresponders. It's very important for the field not to sit back and say we've achieved so much. We have to identify novel drug targets that can help patients who don't respond to currently available treatment, and we have to continue our search for a cure for myeloma."

ELEVATING NURSING ROLES

With Dr. Landgren's arrival at MSK came the introduction of clinical trials nursing roles in myeloma. These nurses work directly with doctors, administrative staff, and research coordinators, helping expand the service's study portfolio with a boost from additional patient care practitioners. "Having strong, independent, clinically experienced research nurses in the clinic every day makes a huge difference for patients and for our service," Dr. Landgren says. "They are superstars."

Without the expertise and efforts of these nurses, the service simply wouldn't be able to handle the 250 to 300 patients currently enrolled in myeloma clinical trials, according to Dr. Landgren. "Currently, every Monday to Friday the entire year, approximately 20 myeloma patients are seen daily in the clinic on a research protocol by a research nurse and a doctor," he explains. "The volume and the pace are high."

Ms. Mastey elaborates further: "Clinical trial nurses support the clinical element of patient care and help with patient advocacy. We're meant to be a liaison between drug companies, doctors, and the administrative team to help develop a trial from early on, and also add a human and clinical element to those studies."

Clinical trial nurses also serve as experts in their own right. MSK's cohort — which may expand to five — attend and speak at national scientific conferences to present the service's work and share ideas with clinical practice nurses from all over the world.

"As a clinical trial nurse, I've felt more empowered than I did by any other role," says Ms. Mastey, who took on this position two years ago. "Every voice is heard here, and no idea is silly or shot down. That's how we're able to think outside the box and push through limits."

PROTOCOL PRIORITIES

With 30 active studies in progress, MSK's myeloma trials span three main research priorities. One is to use genomic testing to identify patients with myeloma precursor disease (so-called high-risk smoldering myeloma), who are at increased an risk of developing multiple myeloma, and to offer early interventions. Another is to develop novel combination therapies to help newly diagnosed multiple myeloma patients achieve minimal residual disease (MRD) with minimal toxicities. A third priority is to develop new drug targets for patients whose myeloma has relapsed or become refractory to treatment.

On all fronts, Dr. Landgren's team has made impressive strides. Several new drugs or drug combinations are being tested for newly diagnosed and relapsed patients, while clinical trials in MRD assays are using the latest cell-, molecular-, and image-based strategies.

Additionally, "We have one of the most advanced CAR T cell myeloma programs in the country — in fact, internationally," he says, referring to the customized immunotherapy that has revolutionized treatment options for certain types of lymphoma and leukemia, and is now being tested in myeloma.

"We have identified novel targets, and we are working on so-called dual-target CAR T cells designed to overcome tumor cell escape," Dr. Landgren continues. "In collaboration with the Cell Therapy Program at MSK, we're

translating our basic research into myeloma patients with high speed. The service is advancing the field rapidly through our leadership in the laboratory as well as the clinic."

Overall, trials are only opened when they match MSK patients' needs and are in areas where MSK's patient volume empowers team members to move forward quickly and deliver results.

"We're working on many first-in-human studies with new targets, bringing new therapies to multiple myeloma patients, which is part of our mission — to have something to offer every patient," Dr. Landgren adds. "We cover all the bases."

But making this happen requires the skills and support of all research staffers, a web of professionals who operate like a finely tuned motor, Ms. Jafri explains.

"We have the appropriate staff in place to run these protocols efficiently and accurately, supporting nurses and investigators and offering quality care for patients," adds Ms. Jafri, who has progressed through a variety of research roles during her decade at MSK. "We're able to support these trials because we have such a robust group."

PATIENTS INSPIRE THE TEAM

In the constant whirl of MSK's myeloma clinical trials — where one study closes and another immediately takes its place — it's the patients and their individual stories that fuel team members' efforts.

"Seeing patients is empowering in itself, and helping someone who may not have had a treatment option before moves us past the day-to-day challenges," Ms. Mastey explains. "With the new drugs in development, we may be able to offer them a new treatment and prolong their life and quality of life. That piece is immediately rewarding.

"Viewed through a wider lens," she continues, "it's incredibly rewarding to know the work we're doing will help people in the future, maybe reshape the disease, and maybe offer patients an improved prognosis. We know that everything we do every day really matters."

Dr. Landgren sees both the reward and responsibility of helping shepherd patients through treatment with a stubborn disease. "Having the opportunity to work with patients is a huge privilege as a human being," he says. But ultimately, he feels that the shared mission among myeloma clinical trial team members as well as everyone at MSK "is what really attracts people to come here, work here, and grow.

"You see so many opportunities where you can make a difference," Dr. Landgren says. "Institutions need people with drive and energy, and we have a group of people who have this kind of vision, who are working forward together." ■

2018 AMERICAN SOCIETY OF HEMATOLOGY MEETING IN SAN DIEGO

From left: Rob Jenq, Alexander Lesokhin, David Chung, and Tsoni Peled

Katharine Hsu (left), James Young, and Jenna Goldberg

Katie Jones (left) and Allison Sams

More than 25,000 people attended the American Society of Hematology (ASH) 2018 annual meeting, with great representation from our division. Research and advances included chimeric antigen receptor (CAR) T cells and the microbiota, CAR T cells for multiple myeloma, targeting peripheral T cell lymphoma, acute myeloid leukemia, smoldering multiple myeloma and the microbiota, and graft-versus-host disease after a bone marrow transplant.

The 11th annual ASH reception for the Division of Hematologic Malignancies was hosted by the Memorial Hospital Alumni Society at the San Diego Marriott Marquis Marina. It was attended by MSK alumni, current faculty, fellows, and colleagues from other institutions as well as invited guests of the division. ■

Q&A
ANTHONY MATO

Anthony Mato came to Memorial Sloan Kettering only a year ago, but he deems it the most productive year in his medical career so far.

MSK's eagerness to develop a clinical trials program in chronic lymphocytic leukemia (CLL) — the most common type of leukemia in the United States — spurred Dr. Mato's recruitment from the University of Pennsylvania, where he directed its CLL program for four years. With startling speed, he and colleagues capitalized on MSK's formal commitment to expanding CLL therapies, opening four new clinical trials since his arrival and expecting a similar number to begin within the next six months.

Additionally, MSK has developed an international registry with a pharmaceutical partner to examine CLL outcomes worldwide (CORE CLL), information that can fuel future clinical trial design. There's also movement toward establishing a tumor bank to answer unforeseen research questions.

"I feel amazed we've been able to get all this done in a relatively short period of time," says Dr. Mato, who sees patients in Manhattan and at MSK Basking Ridge. "MSK is really supportive of the effort. Coming here, I felt I could greatly expand the efforts I'd been making at Penn and that I had a better opportunity to do the type of work I really wanted to do."

Dr. Mato's efforts are inextricably linked with a burst of new developments in CLL in the last five years. A frequent speaker at national and international scientific conferences, he has been instrumental in testing several targeted therapies that have helped move standard CLL treatment past a one-size-fits-all, chemotherapy-based strategy.

MSK doctors devise a personalized approach for each patient from the start by using detailed molecular and genetic profiles to select the most appropriate drugs, which target molecular changes specific to CLL. Dr. Mato and colleagues are now researching whether these drugs work best when used sequentially or combined.

"CLL has been one of the fields within hematologic malignancies where the most progress has been made in developing targeted drugs and chemotherapy-free regimens, more so than any other area," he explains. "When you take together the power of MSK in terms of resources and blend it with the explosion of the field, it has resulted in patients doing better and living longer and is a recipe for huge progress."

In this Q&A, Dr. Mato recounts his path into oncology, as well as his ongoing commitment to patient education and more effective CLL therapies.

What led you into medicine and research?

Medicine was the only thing I ever wanted to do, and oncology within medicine. But leukemia in particular is really the forefront of oncology. Most new treatment paradigms come through patients with hematologic malignancies. To me, it's an area where discoveries happen very quickly and where patients are especially willing to participate in clinical trial efforts. Once I was exposed to it, I knew I would love it.

How do research and patient care mesh in your daily schedule?

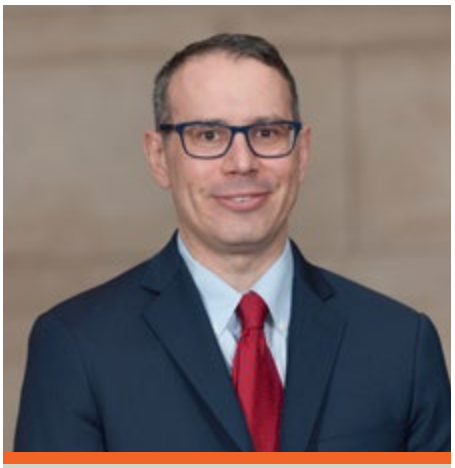
I see patients half the week and perform research and administrative duties the other half. But in my mind, the research questions address the problems we observe in the clinic, such as problems with new therapies or gaps in treatment. We take that information and meet with partners in academia and industry to design studies to solve those problems. For me, it's seamless. I wouldn't be happy taking care of patients without the research aspect, nor would I be happy just doing research. Advancing the field is a wonderful thing, but advancing the care of the patients I'm taking care of is equally important.

You've long been committed to patient education. How are you blending this priority with your role at MSK?

CLL is the most common type of leukemia, so there's some awareness out there but not as much as other malignancies. I'm on the medical advisory board for the CLL Society, and I participate in many events across the region aimed at patient education. We also meet with patients in a more formal way and offer lectures. I also get the word out through online videos, podcasts, and educational interviews. Before I came to MSK, I planned my own events, which sometimes drew around 200 patients. Here, there's a larger patient population and more of a national audience to get our message out.

Why should people with CLL seek care at MSK instead of another institution?

Not only are we committed to state-of-the-art therapies from a clinical trials perspective but we're also committed to state-of-the-art clinical care. It's truly about bringing the best therapies for patients regardless of where they're coming from. At the end of the day, we're driven by the patients coming to MSK and have an unbelievable network of scientists, pathologists, pharmacists, and others also contributing to patient outcomes. By coming here, you're able to access those resources.



"When you take together the power of MSK in terms of resources and blend it with the explosion of the field, it has resulted in patients doing better and living longer and is a recipe for huge progress."

Anthony Mato
Director, Chronic Lymphocytic Leukemia Program, Leukemia Service

What are the biggest challenges remaining in CLL research and treatment?

Our successes have brought forth some key questions. Now that we have all these drugs available, how do we decide the right order to give them? How do we combine them? Is there still a role for chemotherapy for any patient with CLL? For the most part, CLL is still incurable. I'd like to get to a point where we're able to put drugs together to cure patients or control the disease enough where they never have to deal with it again.

What excites you most about your work?

The fact that it's always evolving. Nothing is stagnant, and as things evolve we can see our patients doing better with full knowledge that even ten years ago, many of them wouldn't have been able to survive their disease. As our program grows and we have more of a stake in clinical leadership in CLL — whether in research, guidelines, or patient education — the ripple effects grow. Right now we're small, but our impact has probably quadrupled in the last year. ■

The Department of Medicine management team, from left: Carrie Genrich, Charlie Stein, Erika George, Andrene Samuels, and Brett Wagner

Aaron Goldberg

Elaina Preston

CYCLE FOR SURVIVAL

Memorial Sloan Kettering's Cycle for Survival is a high-energy indoor-cycling event that allows teams of participants to fight rare cancers in a tangible way.

Cycle for Survival is determined to beat rare cancers by powering groundbreaking research to help patients who often have few or no options. With support from our founding partner Equinox, Cycle for Survival had its biggest fundraising year so far in 2018. Raising $39 million this year—and more than $180 million during the last 11 years—was only possible because of our dedicated community of riders, supporters, patients, researchers, and doctors. In 2018, more than 34,000 riders participated across 16 cities. Cycle for Survival was named the PeerToPeer Professional Forum's Program of the Year during its annual conference in 2018. Cycle for Survival supports the advancement of several comprehensive initiatives at MSK, spanning many critical areas of research.

A testament to the spirit of the MSK staff, more than 2,200 members of the MSK community participated as riders or supporters. ■

Teams included:

BSK Med Onc Riders
Cancer Hackers
Dean's Cell Cyclers
DOMinators
PMBL Pulverizers
Straight Outta Chemo
T-cell Racers
Team HOPP – Long Island
Team HOPP Kreb's Cycle
The Mobilizers
The Nutcrackers

MSK SCIENTISTS BUILD "ARMORED" CAR T CELLS TO SMITE SOLID TUMORS

By Matthew Tontonoz

A technological advance may make a cell-based immunotherapy more effective against hard-to-treat cancers.

Scientists at Memorial Sloan Kettering built a new model of genetically engineered immune cells, ones with powerful "armor" that may allow them to fight solid tumors.

The new cells combine two of the most promising types of immunotherapy — chimeric antigen receptor (CAR) T cells and checkpoint inhibitors — into one sleek package. CAR T cells are genetically engineered versions of a patient's own immune cells built to find and kill cancer cells. Checkpoint inhibitors take the brakes off immune cells, allowing them to fight cancer for longer.

"We took a step back and asked, 'How can we make CAR T cells better?' " explains Renier Brentjens, Director of the Cellular Therapeutics Center at MSK and one of the pioneers of CAR therapy. "That's when we decided to try to combine these two promising approaches."

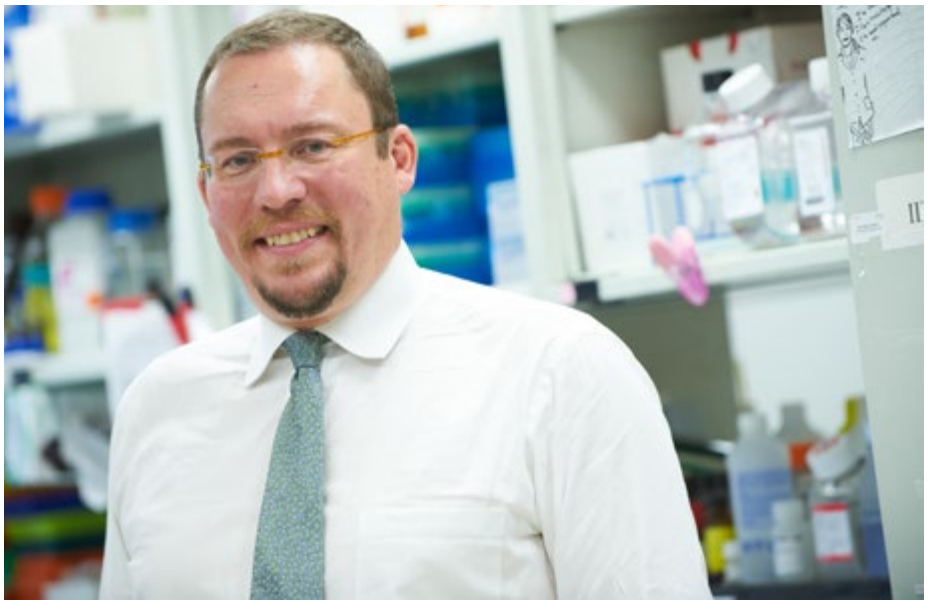
By themselves, CAR T cells have shown remarkable success in treating certain blood cancers. So far, however, they have not been able to vanquish solid tumors. Checkpoint inhibitors, on the other hand, have proven remarkably effective at empowering the immune system to fight a variety of solid tumors. But they can produce severe immune-related side effects.

By engineering checkpoint inhibitors directly into the CAR T cell itself, the MSK team believes they can limit the side effects of these drugs while taking advantage of their powerful immune-stimulating capabilities.

BETTER PERSISTENCE, BETTER RESULTS

The newly designed CAR T cells secrete a mini version of a checkpoint-blocking antibody. This antibody is similar to the drugs nivolumab (Opdivo®) and pembrolizumab (Keytruda®), which are approved for the treatment of several types of cancer. The antibody binds to a protein called PD-1 that acts like a brake on immune cells. The antibody releases this brake, allowing the CAR T cells and surrounding immune cells to better fight the disease.

The MSK team — including lab members Sarwish Rafiq, Oladapo Yeku, and Hollie Jackson — made two versions of this armored CAR. One recognizes a molecule called CD19, which is found on certain blood cancers. The other recognizes MUC16, which is found on some ovarian and pancreatic cancers. Then they tested the cells in several different mouse models of cancer.



Physician-scientist Renier Brentjens leads MSK's Cellular Therapeutics Center, which is pioneering new CAR T cell therapies for people with cancer.

> **"This proves — at least in a mouse model — that we can now have our cake and eat it too."**
>
> Renier Brentjens
> Director of the Cellular Therapeutics Center

In all cases, including mouse models of solid tumors, the team found that the armored CARs persisted longer in the body than standard CARs. And they produced better results — namely, the mice lived significantly longer.

What's more, because the checkpoint drugs were released directly into the tumor, they activated nearby T cells, creating a helpful bystander effect. In other words, the CAR T cells were able to enlist the help of other T cells to fight the tumor.

Finally, the team found that the levels of the PD-1 antibody were low in the circulating blood, indicating that the checkpoint molecules were not spreading far beyond the site of the tumor. That's important because it means there will be fewer systemic side effects.

"This proves — at least in a mouse model — that we can now have our cake and eat it too," Dr. Brentjens says.

He emphasizes that the approach can be thought of as providing a new platform for CAR therapy. "We can build CAR T cells to secrete a variety of different molecules, tailored to the needs of the patient," he says. "It's not just limited to this one drug."

The MSK team hopes to translate their new armored CAR platform to the clinic and is in the process of designing clinical trials.

A paper describing the approach appeared in the journal *Nature Biotechnology*. ■

This study received funding from National Institutes of Health grants (5 P01 CA19017403 and 5 P50 CA19293702), the Canadian Association of New York Foundation's annual Terry Fox Run for Cancer Research in New York City, Kate's Team, the Carson Family Charitable Trust, the William Lawrence and Blanche Hughes Foundation, the Emerald Foundation, the ARD Foundation, and the Center for Experimental Therapeutics at Memorial Sloan Kettering. Dr. Brentjens is a co-founder of and a consultant for Juno Therapeutics, for which he receives royalties.

Q&A
ELIZABETH SCHMIDT RODRIGUEZ

Elizabeth Schmidt Rodriguez
Nursing Director, David H. Koch Center for Cancer Care

To describe Elizabeth Schmidt Rodriguez as a strategic thinker would be a massive understatement.

Joining Memorial Sloan Kettering in 2001 as an oncology nurse and progressing to Nurse Leader in 2005, Ms. Rodriguez continued her education — earning two advanced degrees within five years — while also working closely with leaders in the Division of Hematologic Malignancies to help drive pivotal innovations in the care of MSK patients with blood cancer.

Among other initiatives, Ms. Rodriguez helped develop MSK's groundbreaking outpatient bone marrow transplant (BMT) program, which expanded to include a separate residence for BMT patients on 75th Street more than two years ago.

"From day 1, I've felt that I had this connection to the division and this patient population in my very first job opportunity here," she says.

It's a connection that has not only endured but blossomed. Ms. Rodriguez's extensive contributions to MSK were recognized with her appointment as Nursing Director at the new David H. Koch Center for Cancer Care, an outpatient facility on East 74th Street set to open in November 2019 that will house the entire Division of Hematologic Malignancies.

Taking on this key leadership position reminds Ms. Rodriguez of her transition to Nurse Leader more than a decade ago. A doctor she'd worked with closely at the time asked her, "Why do a management job when you're so good with patients?"

"I told him that sometimes people who leave patient care are burned out, but that was never the case for me," she recalls. "I very much love that direct contact with patients, and sometimes I miss it a little, but I do think in leadership positions we have the opportunity to influence how care is delivered in different ways, and our sphere of influence is larger.

"And I do consider it part of my job to take care of nurses, and they in turn take care of patients," Ms. Rodriguez adds. "In the end, it's really all about people."

In this interview, Ms. Rodriguez explains her transition of duties as opening day nears and the advantages the new outpatient center will offer MSK and its patients.

With the David H. Koch Center for Cancer Care still being built, what are your mix of duties?

I'm focused on working very closely with the design and construction right now. With construction nearly 90 percent complete, I'm over there on a weekly basis providing feedback about where equipment is placed, where to store supplies, the type of chairs clinicians might sit in, and the setup of work stations. A lot of decisions have already been made over the years, but there are still others as we march toward the opening and are in the actual space. Now there's a unified voice from one nursing director who can provide that for the whole building.

The new center is slated to be a "smart building." What does that mean?

We're hoping 23 different informatics initiatives will go live in this building. Examples include location awareness, badgelike devices that will be assigned to everyone in the building, including staff, patients, and caregivers. Once you have a badge, we'll be able to look in the system and see where anyone is in the building at any time. From a patient perspective, we hope that gives them freedom of mobility to see the unique design features throughout the building. From a clinician perspective, it offers an opportunity to collect data, including how long they spend with patients in a room or how long patients spend in the waiting room.

Other technology will include a way-finding app that can help patients navigate through the 750,000-square-foot building, and a parking app that will call for valet parking to bring the car when patients are ready to leave at the end of their visits.

We're hoping to leverage the new technology to augment the care we're providing so patients feel more connected to us. I feel that the things we can often do better are smaller things — we have the big things down pat. But little things — whether we're making sure patients are greeted in a warm and welcoming way when they're entering the building, or navigating to appointments safely and efficiently, or sense their team talking to one another about their care — with those things, we have a real opportunity to move the needle a bit at this new building.

What do you expect a typical day on the job to look like once the new center opens its doors?

In the beginning, I think there will be no typical day, or perhaps far from typical. We're building workflow plans now, but when we get there, we'll have to go back and see if what we expected is actually happening. If it's working, why? And if not, and there are gaps, what are we doing to revise and make that situation better?

I envision not sitting down very much, but walking through the great expanse of space and talking with everyone I come in contact with — patients, staff at all levels — and find out how it's going. Because that's what this building is really all about, the people. I'm really looking forward to engaging with them and moving the mark a bit — taking all the things we're doing so well at MSK and having them implemented there and bringing it up a notch.

What advantages will the David H. Koch Center for Cancer Care bring to MSK?

From a practical perspective, we're bringing a lot of services under one roof. Right now, services that will be located at the center are spread across multiple campuses. Therein lies a good opportunity to collaborate in new ways by having everyone in one building. With collaboration, there's often more synergy and fuel behind efforts to do new things faster or to discover things we haven't thought about before. Doctors and nurses will be able to interact more frequently because they're not spread out in a variety of buildings, and patients won't have to travel to different sites for different types of care. We can do a better job coordinating care more efficiently and seamlessly.

What's the most challenging aspect of your job so far with regards to the Koch Center?

Right now, probably the sheer size and scope of the program and trying to wrap my head around all of the people involved. Sometimes people ask me who are stakeholders — and I answer, "Everybody." It's that big of an effort. ■

LONGEST-RUNNING CAR T TRIAL SHOWS WHICH PATIENTS BENEFIT MOST AND HAVE THE FEWEST SIDE EFFECTS

By Matthew Tontonoz

For adults with relapsed leukemia, chimeric antigen receptor (CAR) T cell therapy is a potentially lifesaving treatment option. A clinical trial conducted at Memorial Sloan Kettering shows the long-term benefit of the approach and suggests ways to make it safer and more effective.

Hematologic oncologist Jae Park cares for people with leukemia and was the principal investigator on a phase I study of CAR T cell therapy in adults with acute lymphoblastic leukemia.

Results from the longest-running clinical trial of CAR T cell therapy for cancer offer key insights into factors affecting the safety and effectiveness of this groundbreaking immunotherapy treatment.

Memorial Sloan Kettering scientists reported in the *New England Journal of Medicine* that adults with acute lymphoblastic leukemia (ALL) who received CAR therapy responded better if they had a small amount of disease at the time of treatment. Compared with people who had a greater amount of disease, those in the low-disease category lived significantly longer and experienced fewer life-threatening side effects.

The eagerly awaited findings were based on an analysis of data from 53 adults with ALL who were treated with CAR therapy at MSK. The maximum follow-up time was five and a half years, with a median of 29 months. The overall median survival was 12.9 months. For those in the low-disease category (defined as less than 5 percent leukemia cells in the bone marrow), the median survival was 20.1 months.

Strikingly, about 50 percent of people in the low-disease category were still alive and well after five years. Doctors speculate that they may be cured.

"This is the longest follow-up study of people with ALL treated with CAR therapy. It confirms the power of CAR T cells as an effective cancer therapy in adults with ALL."

Jae Park
Hematologic Oncologist

"This is the longest follow-up study of people with ALL treated with CAR therapy," says Jae Park, a hematologic oncologist at MSK and the principal investigator of the phase I trial. "It confirms the power of CAR T cells as an effective cancer therapy in adults with ALL. With the long follow-up, we were able to demonstrate for the first time that people with a lower disease burden benefited the most from CAR therapy, with significantly improved survival and reduced toxicity."

Previous studies of CAR therapy in children and adults with ALL had shown impressive initial response rates, ranging from 70 percent to 90 percent. The follow-up data on these groups, however, is limited. Whether people treated with CAR T cells would continue to do well over time has been an open question.

The new results provide the first strong evidence that some people with an otherwise incurable cancer can experience lasting benefits extending to five years or more after receiving a single infusion of CAR T cells. The results also point to specific factors that may influence how well people do on the treatment.

"Among all of the clinical and disease factors we examined, pretreatment disease burden was the strongest predictor of long-term outcome after CAR therapy," Dr. Park says. "Our data suggest that we should give CAR therapy when the disease volume is small to achieve the greatest long-term efficacy and lowest toxicity."

Ultimately, he says, it may make sense for people to receive CAR T cell therapy as a frontline treatment, rather than after other options have failed.

A POWERFUL TREATMENT WITH SERIOUS POTENTIAL SIDE EFFECTS

Doctors and patients alike are excited about CAR therapy because it has proven to be a lifesaving option for very sick people who otherwise would have died from their disease. More than a thousand people in the United States alone have received the immune-based treatment, despite the sometimes severe side effects that can come from supercharging immune cells and releasing them into the body.

Strikingly, about 50 percent of people in the low-disease category were still alive and well after five years. Doctors speculate that they may be cured.

The main potential complication of CAR therapy is cytokine release syndrome (CRS). This powerful surge of immune activity can overwhelm the body's organs and lead to death. Caring for people with CRS requires enormous skill and clinical expertise.

Another potential complication is neurotoxicity, including a dangerous swelling of the brain called cerebral edema. Some CAR trials have been stopped early because there were deaths from cerebral edema. None of these deaths occurred at MSK.

Strikingly, about 50 percent of people in the low-disease category were still alive and well after five years. Doctors speculate that they may be cured.

The results of this study provide important lessons for limiting and managing these side effects. They further show that CAR therapy provides a potential cure for a group of people — adults with relapsed ALL — for whom the US Food and Drug Administration has not approved any CAR T cell treatments.

"This study represents the culmination of 20 years of research at MSK," says Michel Sadelain, Director of the Center for Cell Engineering at MSK and lead author of the study. "These data strongly support the use of this CAR therapy for adults with relapsed ALL and predict better outcomes when used earlier in the course of the disease."

STUDY DETAILS

Patients enrolled on this trial received a single infusion of 19-28z CAR T cells manufactured at MSK. Each person's T cells were isolated from their blood and exposed to a harmless viral vector that inserted the 19-28z CAR gene. The engineered CAR T cells were grown and multiplied in the lab and then infused back into the patient.

Everyone on the study had received multiple previous chemotherapy treatments and either had relapsed or was resistant to further chemotherapy. The rate of complete remission — meaning a leukemia-free state — was 83 percent (44 people). The overall rate of severe CRS was 26 percent (14 people), including one death. The rate of severe neurotoxicity was 42 percent (22 people). There were no cases of fatal neurotoxicity or cerebral edema on the trial.

Some people on the study went on to have a stem cell transplant. Receiving this additional treatment did not correlate with a better outcome.

The analysis of factors affecting the outcome of treatment was retrospective in nature and needs to be confirmed in a prospective trial. MSK investigators hope to open such a trial soon.

ABOUT CAR T CELL THERAPY

The CAR T cells used in this study are built to target a molecule called CD19. This marker is found on the surface of normal and cancerous B cells. MSK scientists were the first to show that CD19 is an optimal target for CAR therapy and played a pioneering role in developing CAR therapy. MSK's CD19 CAR T therapy received a Breakthrough Therapy Designation from the FDA in 2014.

Two commercial CAR T cell therapies are currently approved for use in people: tisagenlecleucel (Kymriah®) for children and young adults with ALL and axicabtagene ciloleucel (Yescarta®) for adults with non-Hodgkin lymphoma.

There is no FDA-approved CAR T cell therapy for adults with ALL. ■

This work was supported by the National Institutes of Health, the Carson Family Charitable Trust, the Emerald Foundation, the Mr. and Mrs. Goodwyn Commonwealth Fund, the Terry Fox Run for Cancer Research organized by the Canadian Association of New York, Kate's Team, the William Laurence and Blanche Hughes Foundation, the Center for Experimental Therapeutics at MSK, Juno Therapeutics, and the Lake Road Foundation.

DR. SEEMA GUPTA ENDOWED VISITING PROFESSOR AND LECTURESHIP

Martin Tallman (right) and the family of Seema Gupta

The Dr. Seema Gupta Endowed Visiting Professor and Lectureship Fund was created by Manjula and Satyendra Gupta in 2017 to honor the memory of their daughter, Seema Gupta. Dr. Gupta completed her fellowship in hematology/oncology at MSK and served as an Attending Physician in the Leukemia and Lymphoma Service from 2001 to 2005. Dr. Gupta suffered a brain injury and subsequently died.

David Avigan

Established as an endowment, this special tribute to the remarkable qualities of Dr. Gupta will extend her legacy as a talented clinician and researcher and is intended to continue in perpetuity. A visiting professor and lectureship in her name will support the visit of a world-renowned leukemia expert to MSK each year.

The inaugural Dr. Seema Gupta Symposium was held on Friday, June 8, 2018. David E. Avigan, a former MSK fellow and currently a professor of medicine at Beth Israel Deaconess Medical Center and Harvard Medical School, served as the keynote speaker. Anthony Daniyan, Andrew Dunbar, Sheng Cai, and Kamal Menghrajani from the Leukemia Service each gave a presentation on their current research efforts. The next Dr. Seema Gupta Symposium will take place Friday, September 27, 2019. ■

MSK REGIONAL NETWORK

Memorial Sloan Kettering provides chemotherapy, radiation treatments, clinical trials, and preoperative and postoperative check-ins at several regional locations.

MSK'S FOOTPRINT ON LONG ISLAND

MSK Nassau, a 114,000-square-foot freestanding cancer treatment center in Nassau County, opened in June 2019. It houses the area's most comprehensive cancer care program and is staffed by a forward-thinking and compassionate healthcare team whose sole focus is caring for people with cancer.

The building and adjacent five-story parking garage neighbor NYCB Live, home of the new Nassau Veterans Memorial Coliseum, which recently underwent a significant transformation of its own. When MSK Nassau opened, MSK closed its Rockville Centre facility and moved its staff and services to the new Nassau facility.

Like other outpatient MSK locations on Long Island and in New Jersey and Westchester County, New York, patients at MSK Nassau benefit from comprehensive cancer services and amenities in a single location. More than 20 cancer doctors covering multiple disciplines — such as medical and radiation oncology, radiology, and surgery — provide the latest in cancer diagnosis and treatment at MSK Nassau. MSK Nassau also provides patients with access to clinical research trials, including phase I trials.

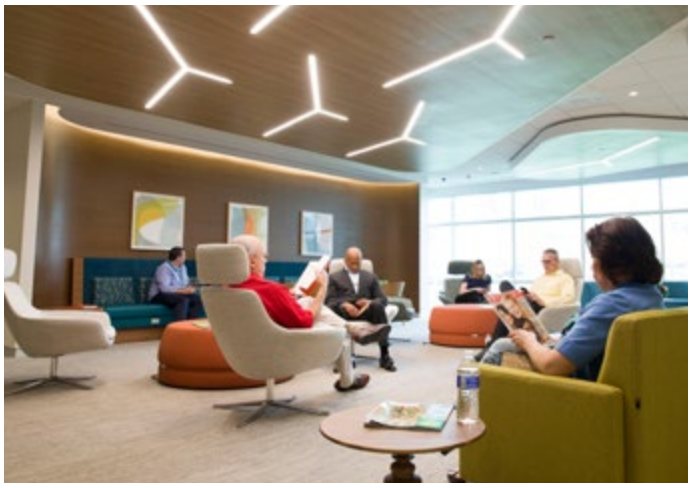
Patients are able to receive much of their treatment — including chemotherapy, immunotherapy, and radiation therapy at MSK Nassau.

The on-site gym at MSK Monmouth is part of a full-service rehabilitative therapy center.

MSK'S PRESENCE IN NEW JERSEY

MSK Monmouth opened its doors in Middletown, New Jersey, in 2016, and the facility has since become a vital part of the community. Now home to about 400 employees, MSK Monmouth is a three-floor facility and spans 26.6 acres. An average of 315 patients come to the site daily to receive the same diagnostic care and treatment that patients receive in Manhattan and our other regional sites. Services include chemotherapy, medical oncology, radiation therapy, radiology and imaging services, surgical consultations, screening services, neuro-oncology, personalized medicine, clinical trials, genetic testing, immunotherapy, support counseling, presurgical testing, and follow-up care. In December 2018, Serena Wong was appointed Regional Care Network Medical Site Director of MSK Monmouth.

In June 2018, MSK Bergen opened in Montvale, New Jersey, offering the same expert cancer care that patients expect from Memorial Sloan Kettering closer to home. At MSK Bergen, residents of Bergen, Essex, Passaic, and Hudson counties in New Jersey, and those living in the lower New York counties of Orange and Rockland, have easier access to the following MSK services: surgical, medical, and radiation oncology consultations; chemotherapy; immunotherapy; radiation therapy; mammography, ultrasound, MRI, CT, and PET imaging; and clinical trials. The facility also offers support groups for patients and educational events for community members and healthcare professionals. In 2018, the 110,000-plus square-foot facility won three awards for its exceptional design and



The waiting area at MSK Bergen is open, airy, and bright with natural light.

Nurses are stationed right outside patient rooms for quick and convenient care at MSK Bergen.

innovative, patient-focused construction: the Adaptive Reuse Award, the IIDA Healthcare Design Award, and the Construction User of the Year Award.

MSK Bergen, MSK Monmouth, and MSK Basking Ridge are members of the Memorial Sloan Kettering–Hackensack Meridian *Health* Partnership, combining both our organizations' expertise to accelerate cancer discoveries, advance clinical care, and improve the lives of the patients. ■

EXPERT CANCER CARE CLOSER TO HOME

HEMATOLOGIC MALIGNANCIES FACULTY CURRENTLY PRACTICING IN THE REGIONAL NETWORK:

Philip Caron*	MSK Westchester
Audrey Hamilton*	MSK Basking Ridge
Hani Hassoun	MSK Westchester
Virginia Klimek	MSK Monmouth
Neha Korde	MSK Basking Ridge, MSK Bergen, and MSK Monmouth
Oscar Lahoud	MSK Commack and MSK Nassau
Sham Mailankody	MSK Commack
Matthew Matasar	MSK Bergen
Anthony Mato	MSK Basking Ridge
Michael Mauro	MSK Bergen
Colette Owens*	MSK Basking Ridge and MSK Monmouth
Ildefonso Rodriguez-Rivera*	MSK Commack
Andrew Zelenetz	MSK Westchester

**Primary location*

MSK CANCER ALLIANCE

The Memorial Sloan Kettering Cancer Alliance is a dynamic and bidirectional collaboration with high-quality community providers.

The aim of the alliance is to enhance access to state-of-the-art cancer care close to home for the alliance members and strategic partners. Through their relationship with MSK, these hospitals want to improve the health and healing of their served communities and provide personalized coordinated care supported by education and clinical research.

The Division of Hematologic Malignancies has been fostering the relationships with alliance hospitals. A key example is the BMT Shared Care program. Research suggests that bone marrow transplant (BMT) is an underutilized definitive therapy for patients with hematologic malignancies, and the timing of a referral for transplant has significant impact on patient outcomes. MSK and Hartford HealthCare Cancer Institute (HHC) developed BMT Shared Care to improve access to transplants, ensure that BMT specialists consult for appropriate candidates during initial treatment planning, reduce burdensome travel for patients by facilitating care locally, and enhance seamless coordination between local oncologists and BMT providers from initial consult though post-transplant care.

Hematologic oncologist Craig Sauter serves as the alliance liaison for BMT Shared Care. He participates in case conferences at HHC monthly to help evaluate whether patients may be potential candidates for transplant. Hematologic oncologist Sergio Giralt helped initiate this program and remains involved. Laura Gastrell is the BMT clinical nurse coordinator focused on BMT intake and pre-transplant care. She works closely with her counterpart at HHC, the BMT nurse coordinator Silvia Willumsen. Since November 2015, there have been 97 referrals for BMT consults, with 41 completed transplants.

The Division of Hematologic Malignancies faculty has sustained relationships with alliance hospitals in other ways as well:

- Physician-scientist Ross Levine visited Lehigh Valley Health Network (LVHN) and HHC to discuss clonal hematopoiesis, an ongoing collaboration.
- Medical oncologist David Solit and Dr. Levine participated in the second annual Lehigh Valley Cancer Institute Symposium on Friday, November 9, 2018.
- Don Park, the new LVHN hematology lead visited MSK on January 22 and 23, 2019, meeting with Chief of the Lymphoma Service Anas Younes and other members of the service, which was an opportunity to highlight engagement with the alliance. ■

Ross Levine and Kelly Bolton (both at center) with members from the Lehigh Valley Health Network

From left: LVHN doctors Usman Shah and Suresh Nair with MSK doctors David Pfister, David Solit, and Ross Levine

THEA NOVICK MERGES THE GOALS OF DOCTORS AND DONORS TO FUND CRUCIAL PROGRAMS

Early in her career, Thea Novick aimed to work for an organization that makes the world a better place.

That's why she knows she's in the right place in her role as Associate Director of Major Gifts for Memorial Sloan Kettering's Office of Development.

Viewing fundraising as a means to improve people, communities, and cultures, Ms. Novick came to MSK about a decade ago, rising through the ranks in Development as she mastered the often-nuanced relationships between doctors and donors. Through major gifts — generally defined as $100,000 and higher — such partnerships help launch research and programs that can greatly improve patients' lives and outcomes.

Most of the donors Ms. Novick works with contribute to the Division of Hematologic Malignancies, and she feels gratified to play a part in moving forward treatment options for blood cancer. But MSK's overall mission is what truly stokes her daily efforts.

"It's such a strong brand and a no-brainer cause because cancer can impact anyone in the entire world, making MSK relevant to everyone," she says. "I feel passionate about maximizing the potential of every person, and MSK's mission is to maximize the potential of people through their health."

"Fundraising is a way to help make services possible that contribute toward positivity," Ms. Novick adds. "Important programs couldn't happen if they weren't funded."

MATCHMAKING: A KEY SKILL

Novick's day-to-day efforts combine working directly with donors while managing a team of five other MSK Development officers. Her frontline fundraising essentially involves matchmaking, merging the needs of researchers — who share details with her about projects that need backing — with the goals and desires of MSK supporters.

"I bridge the information from doctors to potential donors to see if I can identify some common ground so those projects in need of funding might be matched with what philanthropy can provide," she explains. "In managing my relationships with donors, the overarching theme is trying to find prospective donors whose funding interests match with the funding needs of doctors in the division."

"I feel passionate about maximizing the potential of every person, and MSK's mission is to maximize the potential of people through their health."

Thea Novick
Associate Director of Major Gifts
Office of Development

Ms. Novick goes about finding potential donors in a mix of ways. Some donors approach doctors after an impactful experience, such as their own illness or a loved one's, wanting to learn more about their research. Others are past MSK donors whom Ms. Novick contacts to share information on current projects and funding needs. Still others have contributed to similar research at other institutions, whom Ms. Novick proactively pursues to support MSK.

A key part of managing relationships with major donors lies in communication and consistency, she notes.

"We take the time to get to know our donors on a multidimensional level to best connect them with the most relevant projects and keep them apprised of the significant changes their donation has funded," she explains.

CULTIVATING AND PRESERVING RELATIONSHIPS

It's a win-win for Ms. Novick and the division that she concentrates her fundraising efforts on research projects in blood cancer. This way, she develops a familiarity with projects and services within the division. Ms. Novick works closely with each of the division's five service chiefs to keep tabs on new studies and programs.

"I represent the actual science to potential donors on a pretty basic level," she says. "I don't go into huge depth on the technicalities, but I do have some knowledge of terminology and concepts. Usually the doctors themselves represent the most technical aspects of their research, while I'm more focused on the mechanics of making the gift or structuring the gift."

Another key aspect of her role is allowing physicians to preserve doctor-patient relationships with patients who go on to significantly contribute to the physician's research.

"A lot of times patients will say to doctors, 'I'd love to do something to help.' The instinct of the doctor is to tell them to just take care of themselves, but the patient may be a big philanthropist and not know the doctor is being humble and also has a multimillion dollar project that needs funding," Ms. Novick explains.

"Gift officers can represent doctors and MSK regarding the funding needs of their science," she adds. "This way, doctors can keep their focus on their clinical role."

REWARDING ROLE

When Ms. Novick considers the impact her fundraising has had on MSK over the last decade, she's most proud of helping create endowed fellowships that will help train future generations of researchers and clinicians in perpetuity. She's also pleased to have raised funds for MSK's patient financial assistance fund, which she knows has meant a massive difference — and offered huge peace of mind — to patients who otherwise couldn't fully pay for their care.

"Over the nearly ten years I've been here, I feel like I've seen a lot of changes that have helped move forward treatment options for blood cancer," Ms. Novick says. "It's exciting to see the clinical advances that have resulted from the support of philanthropy."

Her momentum seems in no danger either, since Ms. Novick continues to derive immense satisfaction from her job.

"There are so many organizations working to improve the world, and fundraising is such an efficient way to make an impact," she says. "You can tangibly see the dollars come in and help fund impactful projects." ■

HEMATOLOGIC ONCOLOGY TISSUE BANK

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

The HOTB is a centralized, comprehensive resource for banking human biological specimens to support research using primary human cells and tissue. This facility provides appropriate cell- and tissue-based specimens from patients with hematologic and lymphoid malignancies for investigator-initiated experimentation in vitro. These biospecimens are distinct from those handled by the Precision Pathology Biobank Center, because they are not fixed but instead cryopreserved in a manner that allows the recovery of viable cells. Comparable materials are also available from healthy volunteers, although these are more limited in quantity and scope.

When the bank was created, about 150 samples were processed each month. Sample processing has steadily increased, with no signs of slowing down; currently, the HOTB processes more than 2,033 samples per month. The HOTB has an inventory of more than 240,000 aliquots, including peripheral blood components (plasma, serum, granulocyte pellets, and mononuclear cells), buccal swabs for DNA, bone marrow mononuclear cells, skin, and lymphoid tissue.

Research specimens are collected from the following services: Leukemia, Lymphoma, Multiple Myeloma, Bone Marrow Transplant, Pediatrics, Developmental Therapeutics Center, Immunotherapeutics Core, and Dermatology. The MSK regional network sites contribute as well. In addition to tissue banking, the HOTB supports specimen processing for more than 45 clinical trials within MSK. The samples from the HOTB have facilitated research in exploring genetic mutations in cancer diagnoses, testing multiple mass spectrometry–based assays, the xenograft profiling of hematologic malignancies, and many more areas.

The HOTB has become an invaluable resource for biospecimens linked to clinical data annotations. Its value is further enhanced by samples collected both before and after treatment from patients with lymphoid and hematologic malignancies. ■

Front row, from left: Ashley Sauer, Haivy Luu, Jasmine Nicodemus, Annie Slingerland, Mina Louis, and Sean Quach; Back row, from left: Ian McGeary, Zoe Stone-Malloy, Madhu Rangesa, James Young, Sawsan Boutemine, and Mark Pan

MSK CENTER FOR HEMATOLOGIC MALIGNANCIES

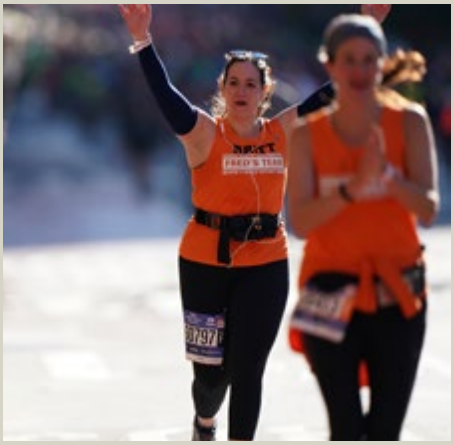
Ross Levine (left), Director of the MSK Center for Hematologic Malignancies, with Aishwarya Krishnan, Research Technician

The Center for Hematologic Malignancies (CHM) serves patients with blood cancer, including leukemia, lymphoma, and myeloma. Our leadership in the field means we are able to support emerging research and move discoveries from the lab to the patient's bedside.

In April 2019, CHM held its second Center of Hematologic Malignancies Scientific Retreat at Mohonk Mountain House in New Paltz, New York. This highly anticipated event fostered interactions between clinical and laboratory investigators to promote translational research and new collaborations. The retreat was attended by 120 CHM members and included formal talks and group discussions aimed at fostering new research directions and interactions. As the keynote speaker, Jonathan Licht, the director of the University of Florida Health Cancer Center, presented on deregulation and oncogenic functions of the NSD2/MMSET histone methyl transferase in hematologic malignancies, and CHM leadership and faculty gave well-received talks on current capabilities, strategic priorities, and new research directions. CHM is planning its next retreat for 2021. ■

Ross Levine

Ross Levine speaks at the prerace dinner.



Brittany Woods

FRED'S TEAM

Fred's Team, named after running legend and founder of the New York City Marathon Fred Lebow, is Memorial Sloan Kettering's athletic fundraising program dedicated to bringing us closer to a world without cancer. By competing in marathons, half-marathons, triathlons, cycling races, and other endurance events worldwide, Fred's Team participants further MSK's pioneering research and support the Aubrey Fund for Pediatric Cancer Research.

More than 900 Fred's Team members took part in the 48th New York City Marathon on November 4, 2018, raising more than $6 million. In total, more than $81 million has been raised since 1995. ■

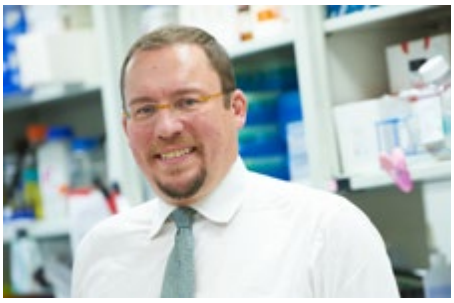
For more information, visit **www.fredsteam.org**.

Participants from the division include:

Rebecca Aviles
Carter Finneran
Elizabeth Giles
Ross Levine
Marcel van den Brink
Brittany Woods

Carter Finneran (right) at the 2018 New York City Marathon

PROMOTIONS



Renier Brentjens

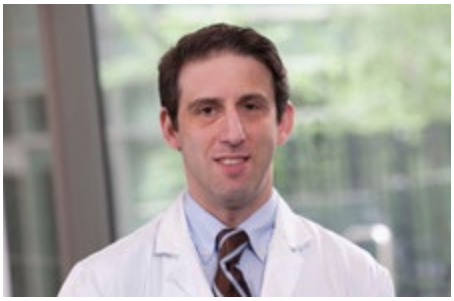
Renier Brentjens was promoted to the rank of Member at MSK, Attending Physician in the Leukemia Service in the Department of Medicine, and Professor of Medicine at Weill Cornell Medical College.

Neha Korde

Neha Korde was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Myeloma Service in the Department of Medicine, and Assistant Professor of Medicine at Weill Cornell Medical College.

Sham Mailankody

Sham Mailankody was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Myeloma Service in the Department of Medicine, and Assistant Professor of Medicine at Weill Cornell Medical College.



Eytan Stein

Eytan Stein was promoted to the rank of Assistant Member at MSK, Assistant Attending Physician in the Leukemia Service in the Department of Medicine, and Assistant Professor of Medicine at Weill Cornell Medical College.

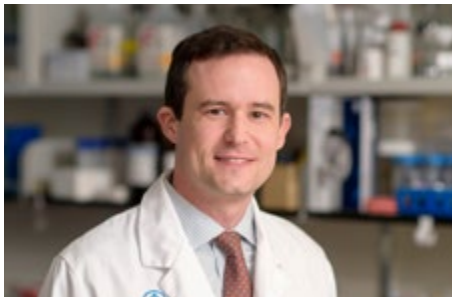
Santosha Vardhana

Santosha Vardhana was promoted to the rank of Assistant Member (Level 1) at MSK, Assistant Attending Physician in the Lymphoma Service in the Department of Medicine, and Instructor of Medicine at Weill Cornell Medical College.

APPOINTMENTS

Kelly Bolton

In July 2018, Kelly Bolton joined the Leukemia Service as an Instructor. Dr. Bolton received a PhD from the University of Cambridge and an MD from the David Geffen School of Medicine at the University of California, Los Angeles. She completed an internal medicine residency at NewYork-Presbyterian Hospital/Weill Cornell Medical Center followed by a medical oncology fellowship at Memorial Sloan Kettering.
Dr. Bolton has created a unique niche in the field of clonal hematopoiesis, which is likely to lead to novel discoveries and contributions to the field of hematologic malignancies as well as cardiovascular diseases. She led in the formation and is the Attending for the Clonal Hematopoiesis Clinic at Memorial Sloan Kettering.



Andrew Dunbar

In August 2018, Andrew Dunbar joined the Leukemia Service as an Instructor. Dr. Dunbar received an MD from New York Medical College and completed his residency at NewYork-Presbyterian Hospital/Weill Cornell Medical Center. He then completed a medical oncology/hematology fellowship at MSK.
Dr. Dunbar's research focuses on identifying the prognostic importance of molecular genetics in acute myeloid leukemia.

Erel Joffe

In September 2018, Erel Joffe joined the Lymphoma Service as an Assistant Attending Physician. Dr. Joffe received an MD from Tel Aviv University and completed an internal medicine residency at Tel Aviv Sourasky Medical Center. Dr. Joffe went on to complete a two-year postdoctoral fellowship in computation biology at the University of Texas Health Science Center and MD Anderson Cancer Center followed by a clinical fellowship in the Department of Hematology and Bone Marrow Transplanation at the Davidoff Cancer Centre in Israel. He then completed research and advanced oncology fellowships at MSK. His research focuses on exploring novel combinations of targeted therapies. He is looking for new biomarkers to help select treatments and precisely identify if and when a disease may relapse in all types of lymphoma.

Kamal Menghrajani

In August 2018, Kamal Menghrajani joined the Leukemia Service as an Assistant Attending Physician. Dr. Menghrajani received an MD from the University of North Carolina, Chapel Hill, and went on to complete an internal medicine residency at the University of Michigan. Dr. Menghrajani then completed a medical oncology/hematology fellowship at MSK, where she served as a chief fellow. Her research focuses on understanding the role of *NRAS* as a driver mutation in secondary AML, using genomics and functional studies and culminating in a clinical trial of targeted therapy.

Ildefonso Ismael Rodriguez-Rivera

In July 2018, Ildefonso Ismael Rodriguez-Rivera joined the Lymphoma Service as an Assistant Attending Physician. Dr. Rodriguez-Rivera received an MD from the University of Texas Southwestern Medical School. He completed a residency in internal medicine at the University of Texas Southwestern Medical School's Austin program, where he was selected as chief resident. Dr. Rodriguez-Rivera then performed a fellowship in hematology and oncology at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, where he also served as a chief fellow. His clinical research focus is in diffuse large B cell lymphoma, indolent non-Hodgkin lymphoma, mantle cell lymphoma, and polycythemia vera.

Gottfried von Keudell

Gottfried von Keudell joined the Lymphoma Service faculty at MSK in May 2018. Dr. von Keudell graduated from the University Hamburg-Eppendorf with MD and PhD degrees. He then completed a research fellowship at Beth Israel Deaconess Medical Center. Dr. von Keudell completed a residency in internal medicine at Boston University Medical Center along with a subsequent fellowship in hematology-oncology at the University of Chicago Medical Center. He was recruited from Yale University School of Medicine to continue investigating the role of novel targeted agents and immune therapies in the treatment of lymphomas and is the principal investigator on several promising early-phase clinic trials.

Cy Wilkins

In April 2018, Cy Wilkins joined the Benign Hematology Service as an Assistant Attending Physician. Dr. Wilkins received an MD from Jefferson Medical College and completed a residency in internal medicine at the University of Southern California. Dr. Wilkins then completed a fellowship in hematology at Boston Medical Center, followed by an advanced fellowship in thrombosis and hemostasis in cancer at MSK. Dr. Wilkins will work in the Benign Hematology Service and provide consultation in the management of bleeding and clotting disorders in people with cancer. His clinical expertise also includes anemia, thrombocytopenia, perioperative anticoagulation, benign blood disorders, and rare blood disorders.

FELLOWSHIP PROGRAMS TRAIN THE LEADERS OF THE FUTURE

Memorial Sloan Kettering attracts applicants from all over the world for its 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 or laboratory investigation. The training program has two main objectives: to provide comprehensive training in the evaluation and care of people 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 or laboratory-based cancer research.

The three-year program, the largest of its kind in the country, attracted more than 500 applicants this past year for just 16 coveted spots. In addition to being outstanding doctors, 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 and impactful scientific publications, and which has allowed our fellows to become leaders in our field in their own right.

BONE MARROW TRANSPLANTATION AND CANCER IMMUNOTHERAPY FELLOWSHIPS

The Adult Hematopoietic Stem Cell Transplantation Fellowship Program at Memorial Sloan Kettering launched in 2007 as an independent, one-year program designed to prepare doctors for academic careers in stem cell transplantation and cellular therapy, 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 and cellular therapy, as well as exposure to the different disciplines that relate to this field. These include radiation oncology and clinical laboratory rotations.

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

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

Since 2007, the program has trained 20 fellows, 18 of whom are now full-time faculty on bone marrow transplantation services in academic centers in the United States and abroad. One graduate is working in the industry as a senior director of clinical research at CRISPR Therapeutics.

Starting in July 2018, the Adult Cancer Immunotherapy Fellowship Program launched. This comprehensive one-year fellowship is designed to prepare doctors who have completed training in medical oncology or hematology for academic careers in cancer immunotherapy. The fellowship is offered jointly by the Adult Bone Marrow Transplantation Service, Cellular Therapeutics Center, and Parker Institute for Cancer Immunotherapy (PICI) at MSK and is supported by the PICI. The structure of the fellowship is similar to the Adult Hematopoietic Stem Cell Transplantation Fellowship, and fellows on the two tracks will benefit from the premier training and research environment at MSK. ■

Hematologist Simon Mantha

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

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

To learn more about immunotherapy fellowships, visit: www.mskcc.org/hcp-education-training/fellowships/adult-cancer-immunotherapy-fellowship-parker-institute-cancer-immunotherapy.

PARKER INSTITUTE FOR CANCER IMMUNOTHERAPY

The mission of the Parker Institute for Cancer Immunotherapy (PICI) at MSK is to accelerate the development of breakthrough immune therapies that are capable of turning cancer into a curable disease.

By bringing together the best scientists, clinicians, and industry partners, in addition to the building a better funding and research model, the Parker Institute provides its members with access to advanced bioinformatics, intellectual property, sequencing, immune monitoring, industry-owned drugs, cell manufacturing, genetic engineering, and clinical trials management.

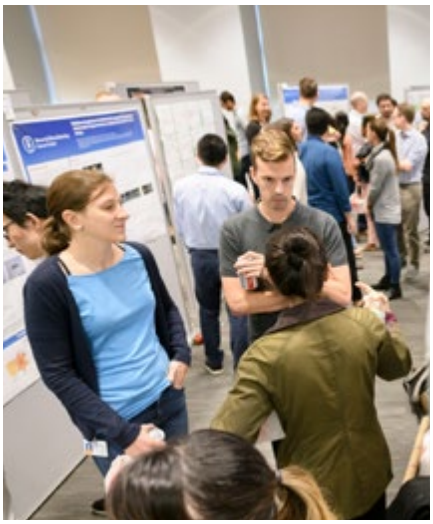
Alan Hanash

Urvi Shah

The PICI runs two internal competition programs at MSK to fund innovative, high-risk ideas related to cancer immunotherapy. In 2018, the center funded nine pilot awards, which are grants of $75,000 each provided as seed money for novel hypotheses. Alan Hanash, Assistant Member and Attending Physician on the Adult Bone Marrow Transplant Service, was a 2018 pilot award recipient.

MSK also participated in the second round of the Parker Institute's Early Career Award program, which awarded $3.1 million in funding to seven recipients in 2018. The goal of the program is to provide funding and resources along with an opportunity to train and interact with top scientists in the field as investigators embark on research to move the field forward. The institute awarded a total of $750,000 to three young investigators as career development awards.

In 2018, PICI established the one-year Adult Cancer Immunotherapy Fellowship Program in collaboration with the Adult Bone Marrow Transplantation Service, Immunotherapeutics Core, and Cellular Therapeutics Center. The fellowship is designed to train hematology oncology doctors in cancer immunotherapy in both inpatient and outpatient settings, with a focus on cell therapy, gene engineering, cancer vaccines, and checkpoint inhibitors. Urvi Shah was the first fellow selected for the program in July 2018. In April 2019, Dr. Shah was recruited to Assistant Member (Level 1) on the Myeloma Service in the Department of Medicine at MSK. ■



Even Rustad (left) and attendees at the 2018 Postdoctoral Research Symposium

Peter and Susan Solomon

SUSAN AND PETER SOLOMON DIVISIONAL GENOMICS PROGRAM

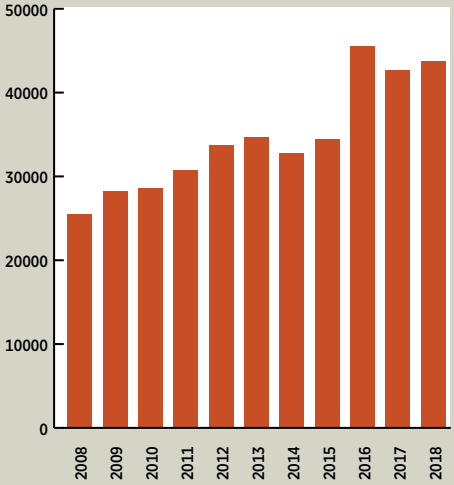
Initiated in 2010, the Susan and Peter Solomon Divisional Genomics Program at MSK is a collaborative, multidisciplinary program.

The program is comprised of clinical and research experts led by Marcel van den Brink, Ross Levine, and Elli Papaemmanuil.

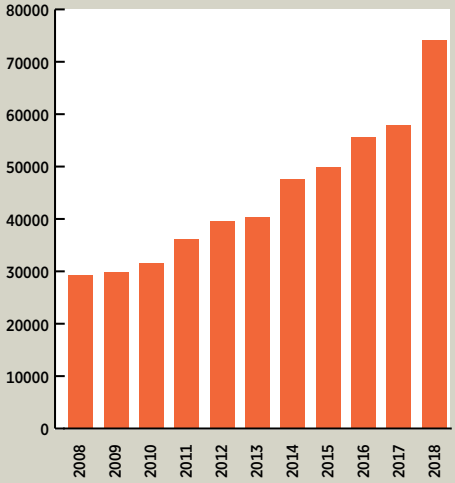
The Solomon Program has continued to support innovative discovery science and translation to the clinic, including genomic profiling of MSK patients with leukemia. This has been used as the basis for mechanism-based clinical trials, directly leading to two clinical trials (IDH2 and IDH1 inhibition) and one AML therapy (enasidenib for IDH2 mutant AML) approved by the US Food and Drug Administration. We have continued to innovate and will soon begin combination therapy trials targeting multiple mutations, which wouldn't be possible without the Solomon Program's support. ■

2018 METRICS

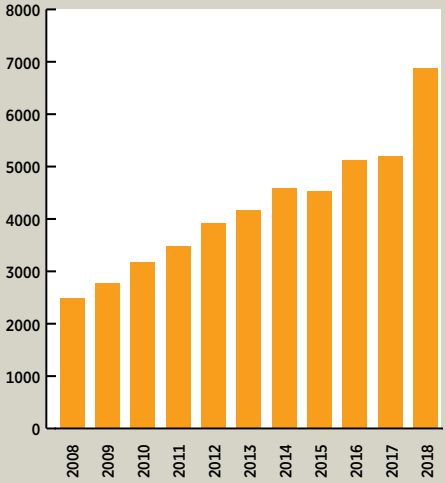
TOTAL INPATIENT VISITS



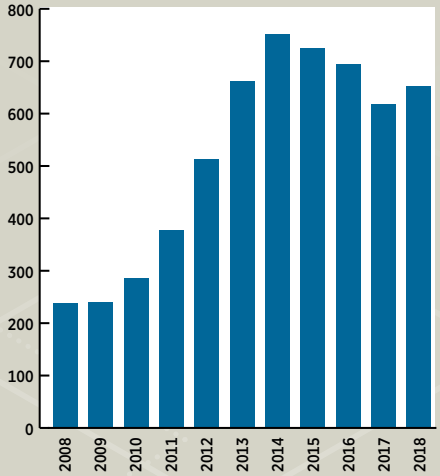
TOTAL OUTPATIENT VISITS



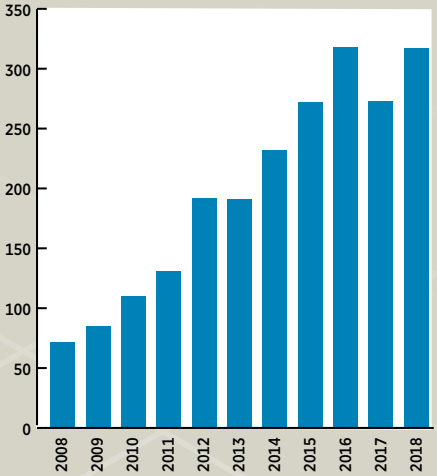
NEW OUTPATIENT VISITS



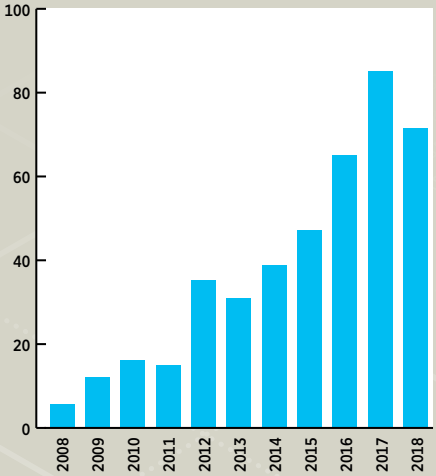
CLINICAL TRIAL ACCRUALS



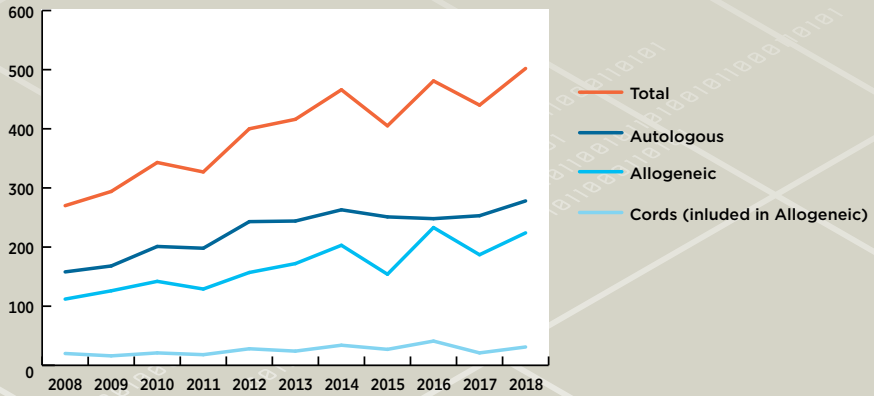
PEER-REVIEWED PUBLICATIONS



AWARDED GRANTS AND CONTRACTS (IN MILLIONS)



ADULT BONE MARROW TRANSPLANTS



HEATHER LANDAU WINS A 2018 MOTHERS OF THE YEAR AWARD

The American Cancer Society named Heather Landau, Associate Attending, a recipient of the 23rd annual Mothers of the Year Award in 2018.

Dr. Landau and Diana Williams, a WABC news anchor, were honored at the Mothers of the Year luncheon on Monday, October 22, at the St. Regis in New York City.

Dr. Landau and Ms. Williams were chosen for their exemplary work in the field of cancer, commitment to philanthropy and the community, and demonstrated compassion for others.

"The work of motherhood, of being a parent, is not one person's work; it's the work of a community, much like the work of caring for patients with cancer," said Dr. Landau at the event. "At MSK, we are part of a collective, a community made up of people who believe in and support a shared goal — to care for patients with cancer. I accept the award on behalf of the many incredible people who make it possible for me to pursue my life's work both inside and outside of the hospital."

Dr. Landau's research focuses on advancing the treatment of plasma cell disorders, including multiple myeloma and light chain (AL) amyloidosis. At MSK, she led the development of the outpatient hematopoietic cell transplantation program, pioneered a homebound transplant initiative using telehealth monitoring, and is studying pharmacokinetically directed melphalan dosing to provide safer and more-effective transplants.

For AL amyloidosis, a disease without a single approved therapy, Dr. Landau has established a comprehensive clinical research portfolio to offer people with this devastating disease treatment and to advance the field.

Having lost her two-year-old daughter, Saige, to drowning in 2015, Dr. Landau took the opportunity at the luncheon to educate the audience about the risk of childhood drowning, the leading cause of death in children ages 1 to 4. She called attention to a program called Water Guardians and urged attendees to use its simple strategy to keep children safe.

Since its establishment in 1995, the Mothers of the Year luncheon has raised more than $5 million for cancer. Previous Mothers of the Year honorees include NBC *Today* show co-host and breast cancer survivor Hoda Kotb, *Today* show co-host Kathie Lee Gifford, Katie Couric, Vera Wang, Ann Curry, and many more.

Congratulations to Dr. Landau on this recognition. ■

Heather Landau with her family

Dr. Landau (fifth from right) with attendees at the 23rd annual Mothers of the Year luncheon

MARTIN TALLMAN ELECTED VICE PRESIDENT OF ASH

The American Society of Hematology (ASH) has elected Martin Tallman, Chief of the Leukemia Service, to the organization's executive committee.

Dr. Tallman is serving a one-year term as Vice President of ASH, which began after ASH's annual meeting in San Diego in December 2018.

Dr. Tallman is one of four new members of the executive committee. He joins Mark Crowther, of McMaster University; Belinda Avalos, of the Levine Cancer Institute and University of North Carolina, Charlotte; and Arnold Ganser, of Hannover Medical School. After completing his one-year term as Vice President of ASH, Dr. Tallman will serve successive terms as President-Elect, then President.

Before coming to MSK in 2010, Dr. Tallman spent more than 20 years as the Director of the Leukemia Program at Northwestern University's Feinberg School of Medicine and Co-Director of the Hematologic Malignancy Program at the Robert H. Lurie Comprehensive Cancer Center and Associate Chief of the Division of Hematology-Oncology at Northwestern University. At MSK, Dr. Tallman's research focuses on acute and chronic leukemia, myelodysplastic syndrome, myeloproliferative neoplasm, stem cell transplantation, hairy cell leukemia, and much more. He was named a top hematologist on Castle Connolly's and *New York* magazine's Top Doctors lists.

Martin Tallman

Dr. Tallman has been a member of ASH for 20 years and has served several leadership roles, including as Councillor. From 2015 to 2016, he served as Co-Chair of the ASH Meeting on Hematologic Malignancies. He will soon complete his three-year term as the executive editor of *Hematology*, ASH's education program book.

To learn more about ASH, visit www.hematology.org. ■

ADVANCE FOR NURSING AWARDS

In 2018, Advance for Nursing conferred its adaptability award, which describes how a team has adapted to a challenge or change and demonstrated the outcomes of that adaptability, to the nursing team at Memorial Sloan Kettering.

M-7 nursing staff

MSK's Bone Marrow Transplant (BMT) Service had been experiencing a rising census challenge. The issue led administration to build a new BMT unit within the hospital (M-7). The question then became: How can MSK develop nurses and ancillary staff who are skilled and equipped to take care of patients on a floor that does not yet exist?

Nurse leaders and advanced practice RNs (APRNs) worked tirelessly to plan an orientation and training program that would cultivate competent staff who would be prepared to take care of these specific patients.

Over a course of ten months, MSK hired a mixture of 40 new BSN graduates and RNs with experience. They received the standard Department of Nursing orientation, which was followed by a BMT-specific didactic and skill orientation held in smaller groups. Nursing leadership, APRNs, and senior staff nurses developed schedules, which consisted of comprehensive lectures and hands-on patient care, including CVC dressing changes, blood product administration, chemotherapy, telemetry, and so on. These group sessions further prepared the new nursing staff to begin their floor orientation.

After completing the lecture and skill training, the new nurses began floor orientations with their preceptors, as is typical for new MSK nurses. However, due to the size of the group, the existing BMT unit could not logistically accommodate everyone. To make things more complex, the new BMT unit would be equipped with telemetry and dialysis, and it would serve people having chimeric antigen receptor (CAR) T cell therapy, none of which the existing unit supported.

Based on these challenges, the team had two goals:

1. To adapt the orientation program to successfully train the new nursing staff to ensure that they would be competent by the time the M-7 BMT unit opened.
2. To create a team while lacking a current designated space

Nursing leadership divided small groups among the three existing floors of the BMT, leukemia, and lymphoma units, which were operational with telemetry. New nurses completed two months of floor orientation on one of the units. Afterward, they rotated to another unit for one month to accommodate the training requirements, and then to the final floor for their last month of orientation.

By splitting and rotating the staff, the new nurses were competently trained in BMT, telemetry, chemotherapy, and CAR T cell therapy. Upon completing four months of floor orientation, the nurses returned to their starting unit and counted in that floor's numbers until the new unit opened.

Throughout orientation, there was continuous communication in staff meetings, by email, and in gatherings with the newly hired staff. Constant communication and personal interaction were chosen as the methods that best nurture a team culture, even though a current team home did not exist.

The newly hired MSK staff were not only trying to learn a complex new role and employment structure, they were also in regularly changing environments and engaging with new staff and culture on each of their rotated orientation floors. Equally, the seasoned staff on the existing units adjusted to the newly hired rotating staff and spent innumerable hours and months orientating all of them to create a team and, ultimately, a successful new BMT unit for MSK's patients.

"Through countless hours of teamwork and constant iteration, we created a strong team that is equipped to take care of our BMT patients on the new floor at MSK," wrote Pamela Hill, Nurse Leader in MSK's submission to Advance. ■

M-7 BMT TEAM

Rebeya Akhtar, UA
Katie Anderson, PCT
Allyson Bagalay, CN I
Jacob Barela, CN I
Tugce Batirbek, CN I
Amanda Bedross, CN I
Jocelyn Brooks, CN II
Camilla Browne, PCT
Kevin Budway, CN IV
Christina Carmi, CN I
Kathy Choo, Clinical Nurse Specialist
Sinead Cormican, CN I
Yvonne Correa, UA
Brianna DiTullio, CN II
Chana Gaerman, CN I
Curtisann Gairy, PCT
Elizabeth Giles, CN I
Neyda Guerrero-Gomez, PCT
Coumba Gueye, PCT
Alison Gurney, CN I
Megan Hall, CN II
Cheryl Haynes, CN I
Pamela Hill, Nurse Leader
Victoria Hohmann, CN I
Stephanie Incardona, CN I
Colleen Johnston-Berresford, CN I
Cherylann Joseph, PCT
Julie Kleber, CN III
Lindsay Lafreniere, CN IV
Jennifer Lee, CN I
Ayelet Lerman, CN I
Zea Levy, PCT
Raffaele Lo Basso, CN II
Natalie Macario, UA
Jacqueline Malabanan, CN I
Katelyn Maldonado, PCT
Diane McCaren, Nursing Professional Development Specialist
Christine McCarthy, CN I
Ryanne McKenna, CN II
Ashley Mercado, UA
Jessica Miller, CN I
Samantha Navarro, CN I
Vivian Ng, CN I
Naebia Nugent, PCT
Rachel Paul, CN I
Kimberly Piruzzi, CN I
Erin Regan, CN I
Lilly Reilly, CN IV
Stephanie Robinson, CN II
Alison Rodriguez, CN I
Lauren Roney, CN I
Joanna Scibilia, PCT
Tara Siebenaller, CN II
Allie Sigadel, CN I
Maureese Thomas, PCT
Tessa Thomas Regis, PCT
Jenny Tran, CN III
Roseanna Troche, CN II
Michael Velazquez,UA
Amber Veritzan, CN I
Adriana Villari, CN I
Sarah Wagner, CN I
Melissa Ward, CN I
Stacey Watson, PCT
Addie Watters, CN II
Phyllis Wilson-John, PCT
Monica Ye, CN I

CN: Clinical Nurse
PCT: Patient Care Technician
UA: Unit Assistant

MORTIMER J. LACHER LECTURE AND FELLOWS CONFERENCE

Mortimer Lacher

Matthew Pianko

Kenneth Anderson

The Ninth Annual Mortimer J. Lacher Lecture and Fellows Conference was hosted by the Division of Hematologic Oncology on May 22, 2018. The event honors Dr. Lacher, a longtime member of MSK'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. In 1965, he published a seminal report with John Durant describing the success of combining vinblastine and chlorambucil to treat Hodgkin's disease.

Dr. Lacher is Co-Founder and current President of the Lymphoma Foundation, and currently serves as a consultant in MSK's Department of Medicine. The Lymphoma Foundation provides annual funding for medical oncology/hematology fellows at MSK as well as specific projects in the laboratories of MSK physician-scientists.

The Ninth Annual Mortimer J. Lacher Lecture, "Targeting Achilles' Heels in Multiple Myeloma," was delivered by Kenneth Anderson, Kraft Family Professor of Medicine at Harvard Medical School as well as Program Director of the LeBow Institute for Myeloma Therapeutics and Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute. He has developed laboratory and animal models of the tumor in its microenvironment that have allowed for both identification of novel targets and validation of novel targeted therapies, and he has rapidly translated these studies to clinical trials culminating in the US Food and Drug Administration's approval of novel targeted therapies. His paradigm for identifying and validating targets in the tumor cell and its milieu has transformed myeloma therapy and markedly improved patient outcomes. ■

Front row, from left: Kamal Menghrajani, Kenneth Anderson, and Niloufer Khan; Back row, from left: Matthew Pianko, Suchit Patel, Ola Landgren, Christopher Hackett, Marcel van den Brink, and Sydney Lu

The 2018 Lacher Fellows are listed below along with their abstracts:

- **Christopher Hackett**
  Mentor: Renier Brentjens

  CD19-Positive Lung Cancer: Optimizing CAR T Cell Therapy in a Clinically Relevant Murine Solid Tumor Model

- **Matthew Pianko**
  Mentor: Alexander Lesokhin

  Exploring the Role of the Microbiota in Multiple Myeloma

- **Sydney Lu**
  Mentor: Omar Abdel-Wahab

  Synthetic Lethality of Splicing Factor Mutant Leukemias with Anticancer Sulfonamide Compounds

- **Kamal Menghrajani**
  Mentor: Martin Tallman

  Drivers of Transformation in Post-MPN AML

- **Suchit Patel**
  Mentor: Joachim Yahalom

  Transcriptomic Characterization Following Cardiac Irradiation Reveals Cell-Type Specific Drivers of Toxicity

- **Niloufer Khan**
  Mentor: Steven Horwitz

  Impact of the Intestinal Microbiome on Outcomes after Autologous Stem Cell Transplantation for Hematologic Malignancy

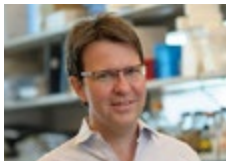
DIVISION AWARDS AND RECOGNITION

The following faculty members received **Steven Greenberg Lymphoma Research Awards**:

Andrew Intlekofer

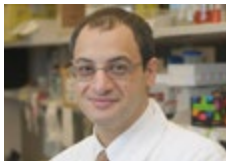
Alison Moskowitz

Dana Tsui



Hans-Guido Wendel

The following faculty members received **Sawiris Foundation Myeloma and Transplant Research Awards**:



Omar Abdel-Wahab

Alexander Lesokhin

Jonathan Peled

Gunjan Shah

Eric Smith

The following faculty in the division received funding from **Cycle for Survival**:

Andrew Intlekofer

Ross Levine

Raajit Rampal

Melody Smith

***New York* magazine's annual "Best Doctors"** list included the following physicians from the division:

Ellin Berman

Martin Tallman

Sergio Giralt

Rekha Parameswaran

Gerald Soff

The following MSK faculty members and fellows in the division received **Young Investigator Awards** from the American Society of Clinical Oncology for these abstracts:

Niloufer Khan
Impact of the Intestinal Microbiome on Outcomes after Autologous Stem Cell Transplantation for Hematologic Malignancies

Sydney Lu
Therapeutic Targeting of RNA Splicing Factor Mutant Leukemias via Inhibiting Protein Arginine Methylation

Kamal Menghrajani
Histone Methyltransferase Inhibitor (Pinometostat) with Azacitidine Combination Therapy in Patients with Relapsed/Refractory MLL-Rearranged Acute Myeloid Leukemia

***Inside Jersey* magazine's "Top Doctors for 2018"** list included:

Audrey Hamilton

LEUKEMIA SERVICE

Omar Abdel-Wahab was elected for membership in the American Society for Clinical Investigation.

Ellin Berman received the Hematology Teaching Award.

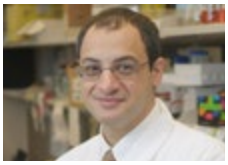
Ross Levine received the William Dameshek Prize from the American Society of Hematology and was elected to the Association of American Physicians. He received a National Institutes of Health Research Project Grant (R01) for *Role of TET2 mutations in malignant transformation and acute myeloid leukemia.*

Jae Park was awarded a Leukemia and Lymphoma Society Translational Research Program grant and an ASH Junior Faculty Scholar Award in Clinical Research.

David Scheinberg received a Doris Duke Charitable Foundation Clinical Research Mentorship Grant.

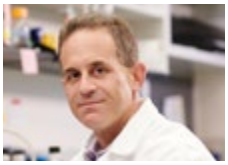
Martin Tallman was elected Vice President of the American Society of Hematology (ASH) and joined the Samuel Waxman Cancer Research Foundation's scientific advisory board.

Aaron Viny received an Independent Scientist Award (K02) from the National Cancer Institute (NCI) for *Role of the cohesin complex in normal and malignant hematopoiesis.*



Omar Abdel-Wahab

Ellin Berman



Ross Levine

Jae Park

David Scheinberg

Martin Tallman

Aaron Viny

ADULT BONE MARROW TRANSPLANT SERVICE

Alan Hanash received an R01 for *Alloreactive and autoreactive immune-mediated mechanisms of impaired epithelial regeneration in the GI tract* and a Parker Institute for Cancer Immunotherapy pilot grant.

Heather Landau received a Mothers of the Year award from the American Cancer Society.

Brian Shaffer received a Mentored Patient-Oriented Research Career Development Award (K23) from the National Heart, Lung, and Blood Institute for *Optimizing NK education and alloreactivity after HLA-haploidentical allogeneic hematopoietic cell transplantation.*

Melody Smith received an ASH–Harold Amos Medical Faculty Development Program Award.

Marcel van den Brink received R01s from the NCI for *The role of intestinal microbiota in graft-versus-host disease* and *endothelial cells regulate immune reconstitution after hematopoietic stem cell transplantation.*

Alan Hanash

Heather Landau

Brian Shaffer

Melody Smith

Marcel van den Brink

LYMPHOMA SERVICE

Andrew Intlekofer was awarded the Damon Runyon Clinical Investigators Award.

Elina Tsyvkin received the Paul Sherlock Faculty Award.

Andrew Intlekofer

Elina Tsyvkin

MYELOMA SERVICE

Eric Smith was awarded a Leukemia and Lymphoma Society Career Development Program grant.

Eric Smith

HEMATOLOGY SERVICE

Rekha Parameswaran received the Hematology Attending Teaching Award for 2018 – 2019 academic year.

Rekha Parameswaran

NURSING AND PHYSICIAN ASSISTANT PUBLICATIONS, PRESENTATIONS, AND RECOGNITION

HONORS

Sheila Kenny serves on MSK's Nurse Practitioner Council.

Lillian Rodich was appointed to MSK's inaugural Physician Assistant Council.

Elaina Preston was appointed Co-Chair of MSK's inaugural APP Professional Development Council.

Amy Pierre was invited to serve on the International Myeloma Foundation's 2019 African American Initiative Advisory Council and served on the International Myeloma Foundation's Nurse Leadership Board.

Elizabeth Halton received the Samuel and May Rudin Award for Excellence in Clinical Trials Nursing.

Susan McCall completed her term of service on MSK's Nurse Practitioner Council.

Gina Abdulahad was elected Communication Chair for the New York State Society of Physician Assistants.

Hilda Quintanilla received the Samuel and May Rudin Award for Excellence in Advanced Nursing Practice.

CERTIFICATIONS

Shani Irby received a doctorate of nursing practice in August 2018.

PUBLICATIONS

Lin RL, Elko TA, Perales MA, Alexander K, Jakubowski AJ, Devlin SM, Dahi PB, Papadopoulos EB, Klimek VM, Giralt SA, Nelson JE. End-of-life care for older AML patients relapsing after allogeneic stem cell transplant at a dedicated cancer center. *Bone Marrow Transplantation*. 2019 May;54(5):700-706. Epub Aug 2018.

Mailankody S, Ghosh A, Staehr M, Purdon TJ, Roshal M, Halton E, Diamonte C, Pineda J, Anant P, Bernal Y, Wills A, Kord N, Lendvai N, Lesokhin AM, Hassoun H, Hultcrantz M, Landau HJ, Shah GL, Scordo M, Chung DJ, Lahoud OB, Khattar P, Fernandez de Larrea C, Gao Q, Jungbluth A, Park JH, Curran KJ, Sauter CS, Palomba ML, Senechal, B, Wang X, Dogan A, Giralt S, Riviere I, Landgren O, Brentjens RJ, Smith EL. Clinical responses anpharmacokinetics of MCARH171, a human-derived BCMA targeted CAR T cell therapy in relapsed/refractory multiple myeloma: final results of a phase I clinical trial. *Blood.* 2018 132:959.

From left: Mariadela Matute (Miami Cancer Institute), Catherine Featherstone (MSK), Stacey Berrios (Miami Cancer Institute), and Erin Frawley (MSK)

Smith M, Littmann ER, Slingerland JB, Clurman A, Slingerland AE, Taur Y, Schluter J, Park JH, O'Cearbhaill R, Mailankody S, Smith EL, Palomba ML, Yeku O, Peled JU, Halton E, Diamonte C, Chan J, Hall M, Anant P, Kane P, Giralt S, Riviere I, Brentjens RJ, Pamer EG, van den Brink MR. Intestinal microbiota composition prior to CAR T cell infusion correlates with efficacy and toxicity. *Blood.* 2018 132:3492.

Park JH, Palomba ML, Batlevi CL, Riviere I, Wang X, Senechal B, Furman RR, Bernal Y, Hall M, Pineda J, Diamonte C, Halton E, Brentjens RJ, Sadelain M. A phase I first-in-human clinical trial of CD19-targeted 19-28z/4-1BBL "armored" CAR T cells in patients with relapsed or refractory NHL and CLL including Richter's transformation. *Blood.* 2018 132:224.

Shah GL, Park JH, Sauter CS, Duck E, Halton E, Palomba ML, Batlevi CL, Younes A, Geyer MB, Smith EL, Mailankody S, Mead E, Santomasso B, Perales M, Sabbatini P, Giralt S, Brentjens RJ, Bach P. Resource utilization early after chimeric antigen receptor (CAR) T cell infusion for hematologic malignancies. *Blood.* 2018 132:616.

McCall SJ. (2018). Case-based management strategies and patient education for cancer immunotherapy. In S. Walker & E. Prechtel Dunphy (Eds.), *Guide to Cancer Immunotherapy* (pp. 241-302). Pittsburgh, PA: Oncology Nursing Forum

Sauter CS, Matasar MJ, Schoder H, Devlin SM, Drullinsky P, Gerecitano J, Kumar A, Noy A, Palomba ML, Portlock CS, Straus DJ, Zelenetz AD, McCall SJ, Miller ST, Courtien AI, Younes A, Moskowitz CH. A phase I study of ibrutinib in combination with R-ICE in patients with relapsed or primary refractory DLBCL. *Blood.* 2018 Apr 19;131(16):1805-1808.

Delacruz A, McCall SJ. (2018). Principles of cancer clinical trials. In C.H. Yarbro, D. Wujcik, & B.H. Gobel (Eds.), *Cancer Nursing* (pp. 227-242). Burlington, MA: Jones & Bartlett Learning.

Ghione P, Moskowitz AJ, De Paola NEK, Horwitz SM, Ruella M. Novel immunotherapies for T cell lymphoma and leukemia. *Curr Hematol Malig Rep*. 2018 Dec;13(6):494-506.

Ginex P, Montefusco M, Zecco G, Trocchia Mattessich N, Burns J, Hedal-Siegel J, Kopelman J, Tan KS. Animal-facilitated therapy program: outcomes from caring canines, a program for patients and staff on an inpatient surgical oncology unit. *Clin J Oncol Nurs*. 2018 Apr 1;22(2):193-198.

ABSTRACTS, POSTERS, AND PRESENTATIONS

Sheila Kenny presented *Impact of Hematopoietic Stem Cell Transplant (HSCT) Vitamin D Algorithm on Vitamin D Levels of HSCT Patients — Part II* at the BMT Nursing Oral Abstracts session at the BMT Tandem Meetings.

Elaina Preston presented the poster *Disease Progression Is Main Barrier to Allogeneic Hematopoietic Stem Cell Transplant in Patients with Newly Diagnosed and Relapsed Acute Leukemia* at the ASBMT and EBMT meetings and the poster *Rituximab Use, Immune Reconstitution, and Vaccination after Ex-Vivo CD34- Selected Myeloablative Allogeneic Hematopoietic Cell Transplantation (HCT)* at the ASBMT meeting.

Amy Pierre presented a webinar with Sikander Ailawadhi from the Mayo Clinic and Wendy Cozen from the University of Southern California entitled *Multiple Myeloma in African Americans: Understanding Differences in Incidence and Treatment*.

Elizabeth Halton presented the abstract *Running the "CAR" Shop: Nursing's Role in Establishing the Intake and Management Standards of Patients Enrolled in CAR T Cell Clinical Trials* at the Oncology Nursing Conference.

Susan McCall presented *Updates in Hodgkin Lymphoma* at the Lymphoma and Myeloma International Congress on Hematologic Malignancies and *N364 Cancer Case Study* at the University of Pennsylvania, Undergraduate School of Nursing.

Anita Kumar, Andrew Zelenetz, Connie Lee Batlevi, Philip Caron, Ahmet Dogan, Pamela Drullinsky, John Gerecitano, Audrey Hamilton, Paul Hamlin, **Leana Laraque**, Matthew Matasar, **Susan Jennifer McCall**, Alison Moskowitz, Craig Moskowitz, Colette Owens, **Janine Pichardo**, Heiko Schöder, **Allison Sigler**, David Straus, and Anas Younes presented the poster *Initial Results of a Phase II Study of Sequential Chemotherapy and Lenalidomide Followed by Rituximab and Lenalidomide Maintenance for Untreated Mantle Cell Lymphoma* at ASH.

Gina Abdulahad was among the invited faculty who presented *How to Survive PA School* to PA students at the NYSSPA conference.

Kevin O'Hara made three presentations at the AAPA conference:

- *Advanced Case Studies in Sexually Transmitted Infections* (co-presented with Jonathan Baker)
- *HIV Case Studies for the Primary Care and GYN Clinician*
- *Syphilis and Lyme: A Tale of Two Spirochetes*

Elizabeth Rodriguez (left) and Karen Collum

Jason Carter presented *The APP Role in the Conduct of a Phase I Trial of a Novel PI3K Inhibitor* at the MSK Cancer Alliance CME symposium "Innovations in Personalized Oncology."

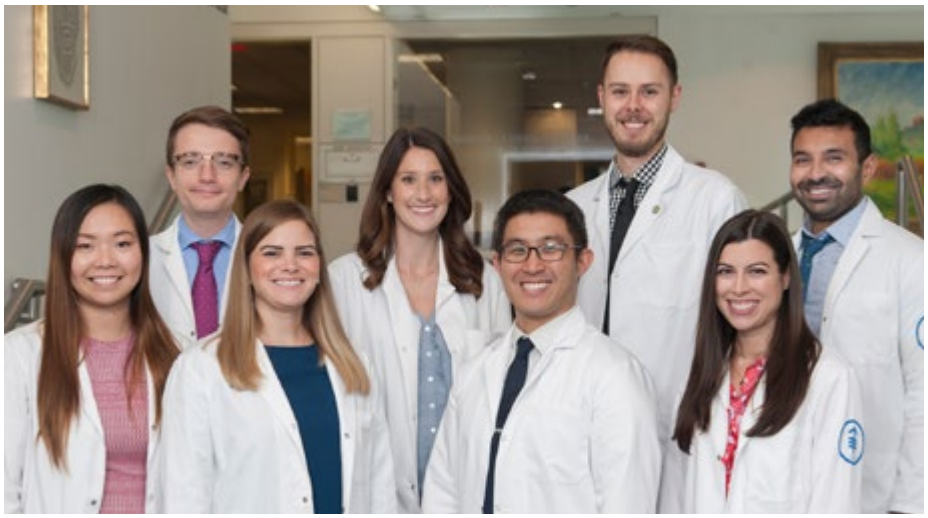
Christina Kiss presented *Transition of Care: Outpatient to Homebound HCT* at the NCCN nursing forum.

Nancy Cruz Sitner presented *BMT Trivia — Let's Recap* at the weekly BMT education series.

Patrice Hunter presented *Cardiac Complications of HSCT* at the weekly BMT education series.

Inpatient nurses at the 2018 Nursing Social

PHARMACY PUBLICATIONS, PRESENTATIONS, AND RECOGNITION



BMT Clinical Pharmacy Team
From left: Carmen Lau, Bradley Figgins, Meagan Griffin, Kathryn Maples, Andrew Lin, Anthony Proli II, Lauren DeRespiris, and Valkal Bhatt

PUBLICATIONS

Vasan N, Carlo M, Drilon A, **King AC**, et al. Pocket Oncology (Second Edition). Anthracycline, Small Molecular Inhibitor, and Novel Anticoagulant Chapters. Wolters Kluwer. 2018

Stump SE, et al. Cabozantinib-induced serum creatine kinase elevation and musculoskeletal complaints. *Investigational New Drugs*. 2018;36(6):1143-1146. doi:10.1007/s10637-018-0629-2.

Xiao W, Goldberg AD, Famulare C, Devlin S, Nguyen N, Sim S, **Kabel CC**, et al. Loss of plasmacytoid dendritic cell differentiation is highly predictive for post-induction measurable residual disease and inferior outcomes in acute myeloid leukemia. *Haematologica*. 2018; 403.

Bange E, Timlin C, **Kabel C**, et al. Evidence for and against green tea and turmeric in the management of chronic lymphocytic leukemia. *Clinical Lymphoma, Myeloma & Leukemia*. 2018; 18(10):e421-6.

Tang LA, **Dixon BN**, **Maples KT**, Poppiti KM, **Peterson TJ**. Current and investigational agents targeting the PI3K (phosphoinositide 3-kinase) pathway. *Pharmacotherapy*. 2018 Aug 18. doi: 10.1002/phar.2173. Epub ahead of print.

Maples KT, Sabo RT, McCarty JM, Toor AT, Hawks KG. Maintenance azacitidine after myeloablative allogeneic hematopoietic cell transplantation for myeloid malignancies. *Leuk Lymphoma*. 2018;4:1-6. doi:10.1080/10428194.2018.1443334. Epub ahead of print.

Bhatt V. Current market and regulatory landscape of biosimilars. *American Journal of Managed Care*. 2018; S451-456.

Buege MJ, DiPippo AJ, DiNardo CD. Evolving treatment strategies for elderly leukemia patients with IDH mutations. *Cancers (Basel)*. 2018 Jun 6;10(6).

Nightingale G, Schwartz R, Kachur E, **Dixon BN**, Cote C, Barlow A, Barlow B, Medina P. Clinical pharmacology of oncology agents in older adults: a comprehensive review of how chronologic and functional age can influence treatment-related effects. *J Geriatr Oncol*. 2018 Jul 13. doi: 10.1016/j.jgo.2018.06.008. Epub ahead of print.

Pastores SM, Goldman DA, Shaz DJ, Kostelecky N, **Daley RJ, Peterson TJ**, Tan KS, Halpern NA. Characteristics and outcomes of patients with hematologic malignancies receiving chemotherapy in the intensive care unit. *Cancer*. 2018 Jul 15;124(14):3025-3036.

Xiao W, Yabe M, Offin M, Khattar P, Baik J, **Daley RJ**, et al. Evolution of a chemosensitive core-binding factor AML into an aggressive leukemia with eosinophilic differentiation. *Blood Advances* 2018;2:1517-21.

Horvat TZ, Seddon AN, Ogunniyi A, **King AC**, Buie LB, **Daley RJ**. The ABCs of immunotherapy for adult patients with B-cell acute lymphoblastic leukemia. *Ann Pharmacother* 2018 Mar;52(3):268-276.

POSTER PRESENTATIONS

King AC, et al. Blinatumomab with concurrent oral tyrosine kinase inhibitor therapy is a well-tolerated consolidation strategy and eradicates measurable minimal residual disease in adults with philadelphia chromosome positive acute lymphoblastic leukemia. Poster presented at: American Society of Hematology Annual Meeting; December 2018; San Diego, CA.

Geyer MB, Burke PW, **King AC**, et al. Ruxolitinib in combination with dasatinib and dexamethasone is an active and well-tolerated chemotherapy-sparing oral induction regimen for adults with philadelphia chromosome positive ALL: results of a phase I trial. Poster presented at: American Society of Hematology Annual Meeting; December 2018; San Diego, CA.

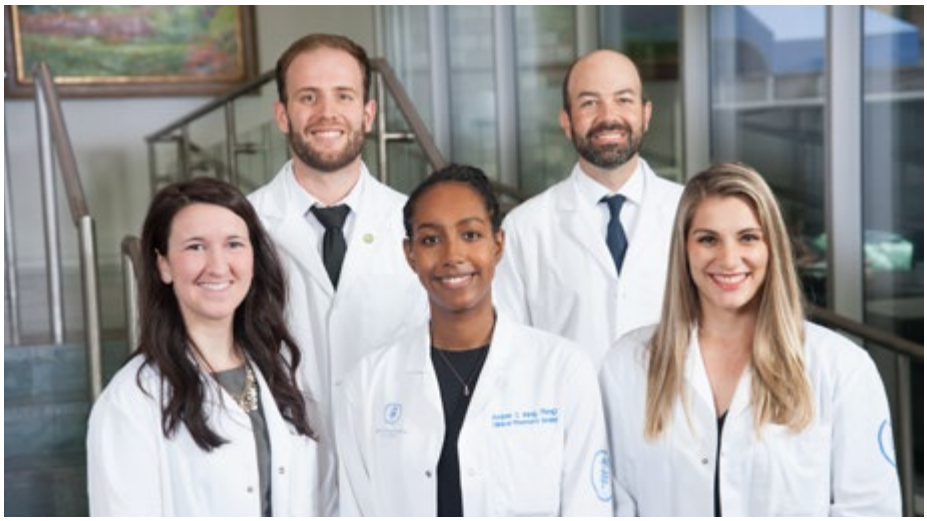
Rampal, RR, Verstovsek S, Devlin S, **King AC**, et al. Early results of a phase II study of combined ruxolitinib and thalidomide in patients with myelofibrosis. Poster presented at: American Society of Hematology annual meeting; December 2018; San Diego, CA.

Stump, SE, et al. Evaluation of mobilization efficacy with an extended interval following plerixafor administration. Poster presented at: Hematology/Oncology Pharmacy Association Annual Meeting; March 2018; Denver, CO.

Griffin M, Zheng J, **Lin A**, Maloy M, Glezerman I, Jakubowski A. Outcomes in elderly hematopoietic stem cell transplant patients receiving tacrolimus graft-versus-host disease prophylaxis. Poster presented at: American Society of Blood and Marrow Transplantation Annual Meeting; February 2018; Salt Lake City, UT.

Lau C, Politikos I, Devlin S, et al. Analysis of cytomegalovirus (CMV) infections in the first 180 days in adult sero-positive cord blood transplantation (CBT) recipients reveals high infection rates and treatment burden. Poster presented at: American Society of Blood and Marrow Transplantation Annual Meeting; February 2018; Salt Lake City, UT.

Pearl N, **Lin A**, Hilden P, Buie LW, Robinson K, Maloy M, Shah G. Effect of obesity on the efficacy and toxicities in patients undergoing autologous hematopoietic stem cell transplant (AHCT) form lymphoma. Poster presented at: American Society of Hematology Annual Meeting and Exposition; December 2018; San Diego, CA.



Leukemia Clinical Pharmacy Team
From left: Sarah Stump, Jeremy Pappacena, Amber King, Ryan Daley, and Charlene Kabel

Lymphoma and Multiple Myeloma Clinical Pharmacy Team
From left: Jennifer Orozco, Brianne Dixon, Tim Peterson, Michael Buege, and Terry Pak

Lin A, Hilden P, Maloy M, Jakubowski A, Papadopoulos E, Sauter C, Tamari R, Ponce D, Giralt S, Gyurkocza B. Impact of omitting post-transplant mini-methotrexate doses in allogeneic hematopoietic cell transplant: a single-center retrospective study. Poster presented at: American Society of Blood and Marrow Transplantation Annual Meeting; February 2018; Salt Lake City, UT.

Bhatt V, Diamond E, Hilden P, Landau H, et al. Engraftment syndrome following high dose therapy and autologous hematopoietic cell transplantation (AHCT) in patients with multiple myeloma and light chain (AL) amyloidosis. Poster presented at: European Society for Blood and Marrow Transplantation Annual Meeting; March 2018; Lisbon, Portugal.

Bhatt V, Diamond E, Hilden P, Landau H, et al. Engraftment syndrome following high dose therapy and autologous hematopoietic cell transplantation (AHCT) in patients with multiple myeloma and light chain (AL) amyloidosis. Poster presented at: International Symposium on Amyloidosis; March 2018; Kumamoto, Japan.

Buege M, Marx K, Shelburne S, Aitken S. Cefepime minimum inhibitory concentration and clinical outcomes in leukemia patients with pseudomonas aeruginosa bloodstream infections. Poster presented at: Hematology/Oncology Pharmacy Association Annual Meeting; March 2018; Denver, CO.

Bhatt V, Buie L, **Pappacena J,** et al. Bu/Mel/Flu conditioning versus HFTBI/Thio/Cy based conditioning in patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) undergoing CD34-selected T-cell depleted allogeneic stem cell transplantation (alloSCT). Poster presented at: Hematology/Oncology Pharmacy Association Annual Meeting; March 2018; Denver, CO.

Pak T, Offin M, Drilon A, et al. Clinical characteristics and treatment-related outcomes for patients with non-small cell lung cancers (NSCLC) harboring BRAF non-V600 mutations. Poster presented at: Hematology/Oncology Pharmacy Association Annual Meeting; March 2018; Denver, CO.

Dixon B, **Daley R**, Buie L, et al. IL-6 and Hyponatremia with the use of CD-19+ CAR T-cell. Poster presented at: Onco-Nephrology Symposium; December 2018; Houston, TX.

NATIONAL PRESENTATIONS

Amber King was an invited speaker at JADPRO Live; she presented *CAR T Cell Therapy and the Pharmacology of Managing Cytokine Release Syndrome*.

Kathryn Maples presented the abstract *Maintenance Azacitidine after Myeloablative Allogeneic Hematopoietic Cell Transplantation for Myeloid Malignancies* at the BMT Tandem Meetings.

NATIONAL COMMITTEE REPRESENTATION

Ryan Daley was appointed to the Alliance for Clinical Trials in Oncology's Pharmacy Committee.

Kathryn Maples is a member of ASTCT's Pharmacy Special Interest Group's Communications Working Committee, and the Hematology/Oncology Pharmacy Association's Membership Committee.

Valkal Bhatt was elected Bone Marrow Transplant Chair for the Clinical Trials Network's Pharmacy Committee and Pharmacy Group Chair for the International Society for Cell and Gene Therapy's APP and Pharmacy Special Interest Group.

Brianne Dixon serves on the Lymphoma Research Foundation's Fundraising Committee.

PUBLICATIONS

These are a few of the 318 peer-reviewed articles published by the division's faculty in 2018 and early 2019.

HEMATOLOGY

NCCN guidelines insights: cancer-associated venous thromboembolic disease, version 2.2018.

Streiff MB, Holmstrom B, Angelini D, Ashrani A, Bockenstedt PL, Chesney C, Fanikos J, Fenninger RB, Fogerty AE, Gao S, Goldhaber SZ, Gundabolu K, Hendrie P, Lee AI, Lee JT, Mann J, McMahon B, Millenson MM, Morton C, Ortel TL, Ozair S, Paschal R, Shattil S, Siddiqi T, Smock KJ, Soff G, Wang TF, Williams E, Zakarija A, Hammond L, Dwyer MA, Engh AM.

J Natl Compr Canc Netw. 2018;16(11):1289-303. PMID: 30442731.

This manuscript is the updated NCCN guidelines for management of venous thromboembolism in people with cancer. This represents the standard of care.

Use of direct oral anticoagulants for treating venous thromboembolism in patients with cancer.

Soff GA.

J Natl Compr Canc Netw. 2018;16(5S):670-3. PMID: 29784753.

This manuscript summarizes the overall guideline by the NCCN committee on cancer-associated venous thromboembolic disease. This represents the standard-of-care guidelines and recommendations for cancer-associated thrombosis.

Predictive factors of fatal bleeding in acute promyelocytic leukemia.

Mantha S, Tallman MS, Devlin SM, Soff GA.

Thromb Res. 2018;164 Suppl 1:S98-S102. PMID: 29703492.

This manuscript highlights that acute promyelocytic leukemia (APL) is associated with primary hyperfibrinolysis and that white blood cell count is a predictor of hemorrhagic early death in APL.

Role of direct oral anticoagulants in the treatment of cancer-associated venous thromboembolism: guidance from the SSC of the ISTH.

Khorana AA, Noble S, Lee AYY, Soff G, Meyer G, O'Connell C, Carrier M.

J Thromb Haemost. 2018 Sep;16(9):1891-1894. PMID: 30027649.

This manuscript is the updated International Society on Thrombosis and Haemostasis guidelines for the management of venous thromboembolism in people with cancer. This represents the standard of care.

Regulatory BC200 RNA in peripheral blood of patients with invasive breast cancer.

Iacoangeli A, Adzovic L, Chen EQ, Latif Cattie R, Soff GA, Tiedge H.

J Investig Med. 2018 Oct;66(7):1055-1063. PMID: 29967012.

This study represents the characterization of the BC200 RNA as a potential new biomarker for breast cancer.

LYMPHOMA

Isoform switching as a mechanism of acquired resistance to mutant isocitrate dehydrogenase inhibition.

Harding JJ, Lowery MA, Shih AH, Schvartzman JM, Hou S, Famulare C, Patel M, Roshal M, Do RKG, Zehir A, You D, Selcuklu SD, Viale A, Tallman M, Hyman DM, Reznik E, Lydia WS, Finley LWS, Papaemmanuil E, Tosolini A, Frattini MG, MacBeth KJ, Liu G, Fan B, Choe S, Wu B, Janjigian YY, Mellinghoff IK, Diaz LA, Levine RL, Abou-Alfa GK, Stein EM, Intlekofer AM.

Cancer Discovery, 2018 Dec;8(12):1540-1547. PMID: 30355724.

Here, we describe four clinical cases that identify mutant IDH isoform switching, either from mutant IDH1 to mutant IDH2 or vice versa, as a mechanism of acquired clinical resistance to IDH inhibition in solid and liquid tumors. IDH-mutant cancers can develop resistance to isoform-selective IDH inhibition by "isoform switching" from mutant IDH1 to mutant IDH2 or vice versa, thereby restoring 2HG production by the tumor. These findings underscore a role for continued 2HG production in tumor progression and suggest therapeutic strategies to prevent or overcome resistance.

Rituximab plus lenalidomide in advanced untreated follicular lymphoma.

Morschhauser F, Fowler NH, Feugier P, Bouabdallah R, Tilly H, Palomba ML, Fruchart C, Libby EN, Casasnovas RO, Flinn IW, Haioun C, Maisonneuve H, Ysebaert L, Bartlett NL, Bouabdallah K, Brice P, Ribrag V, Daguindau N, Le Gouill S, Pica GM, Martin Garcia-Sancho A, López-Guillermo A, Larouche JF, Ando K, Gomes da Silva M, André M, Zachée P, Sehn LH, Tobinai K, Cartron G, Liu D, Wang J, Xerri L, Salles GA.

N Engl J Med. 2018 Sep 6;379(10):934-947. PMID: 30184451.

Rituximab plus chemotherapy has been shown to be effective in patients with advanced-stage, previously untreated follicular lymphoma; nevertheless, most patients will have a relapse. Combination immunotherapy with lenalidomide and rituximab is an immunomodulatory regimen that has shown promising activity in patients with indolent B cell non-Hodgkin lymphoma. Here, we conducted this international, multicenter phase III superiority trial to evaluate rituximab plus lenalidomide, as compared with rituximab plus chemotherapy, in patients with previously untreated follicular lymphoma. Among patients with previously untreated follicular lymphoma, efficacy results were similar with rituximab plus lenalidomide and rituximab plus chemotherapy (with both regimens followed by rituximab maintenance therapy). The safety profile differed in the two groups.

Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial.

Horwitz S, O'Connor OA, Pro B, Illidge T, Fanale M, Advani R, Bartlett NL, Christensen JH, Morschhauser F, Domingo-Domenech E, Rossi G, Kim WS, Feldman T, Lennard A, Belada D, Illés Á, Tobinai K, Tsukasaki K, Yeh SP, Shustov A, Hüttmann A, Savage KJ, Yuen S, Iyer S, Zinzani PL, Hua Z, Little M, Rao S, Woolery J, Manley T, Trümper L; ECHELON-2 Study Group.

Lancet. 2019 Jan 19;393(10168):229-240. PMID: 30522922. Epub 2018.

Frontline treatment with A+CHP is superior to CHOP for patients with CD30-positive peripheral T cell lymphoma as shown by a significant improvement in progression-free survival and overall survival with a manageable safety profile.

CALGB 50604: risk-adapted treatment of nonbulky early-stage Hodgkin lymphoma based on interim PET.

Straus DJ, Jung SH, Pitcher B, Kostakoglu L, Grecula JC, Hsi ED, Schöder H, Popplewell LL, Chang JE, Moskowitz CH, Wagner-Johnston N, Leonard JP, Friedberg JW, Kahl BS, Cheson BD, Bartlett NL.

Blood. 2018 Sep 6;132(10):1013-1021. PMID: 30049811.

Researcher Melody Smith (right) and graduate student Pamela Hatfield

A negative interim PET/CT after one to three cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) in patients with newly diagnosed, nonbulky stage I or II Hodgkin lymphoma (HL) predicts a low relapse rate. This phase II trial was designed to determine if a population of patients with early-stage disease can be treated with short-course ABVD without radiation therapy on the basis of a negative interim PET/CT, thereby limiting the risks of treatment. Four cycles of ABVD resulted in durable remissions for a majority of patients with early-stage nonbulky HL and a negative interim PET.

NOXA genetic amplification or pharmacologic induction primes lymphoma cells to BCL2 inhibitor-induced cell death.

Liu Y, Mondello P, Erazo T, Tannan NB, Asgari Z, de Stanchina E, Nanjangud G, Seshan VE, Wang S, Wendel HG, Younes A.

Proc Natl Acad Sci USA. 2018 Nov 20;115(47):12034-12039. PMID: 30404918.

BCL2 selective inhibitors are promising agents currently under clinical investigation for treatment of BCL2-dependent cancers. However, the clinical activity of BCL2 inhibitors in patients with diffuse large B cell lymphoma (DLBCL) has been disappointing. In this study, we identified PMAIP1/NOXA gene amplification as a marker of sensitivity to BCL2 inhibitors in DLBCL. Cells lacking NOXA amplification were less sensitive to BCL2 inhibitors due to co-dependency on MCL1 and BCL2 proteins. We show that pharmacologic induction of NOXA by the HDAC inhibitor panobinostat primes DLBCL to BCL2 inhibitor-induced cell death by disrupting the co-dependency on BCL2 and MCL1, mimicking the biologic effects of NOXA genetic amplification. Our data provide a mechanistic rationale for combining HDAC inhibitors with BCL2 inhibitors in DLBCL.

LEUKEMIA

Long-Term follow-up of CD19 CAR therapy in acute lymphoblastic leukemia.

Park JH, Rivière I, Gonen M, Wang X, Sénéchal B, Curran KJ, Sauter C, Wang Y, Santomasso B, Mead E, Roshal M, Maslak P, Davila M, Brentjens RJ, Sadelain M.

N Engl J Med. 2018 Feb 1;378(5):449-459. PMID 29385376.

CD19-specific chimeric antigen receptor (CAR) T cells induce high rates of initial response among patients with relapsed B cell acute lymphoblastic leukemia (ALL) and long-term remissions in a subgroup of patients.

We conducted a phase 1 trial involving adults with relapsed B cell ALL who received an infusion of autologous T cells expressing the 19-28z CAR at Memorial Sloan Kettering. Safety and long-term outcomes were assessed, as were their associations with demographic, clinical, and disease characteristics.

Acquired resistance to IDH inhibition through trans or cis dimer-interface mutations.

Intlekofer AM, Shih AH, Wang B, Nazir A, Rustenburg AS, Albanese SK, Patel M, Famulare C, Correa FM Takemoto N, Durani V, Liu H, Taylor J, Farnoud N, Papaemmanuil E, Cross JR, Tallman MS, Arcila ME, Roshal M, Petsko GA, Wu B, Choe S, Konteatis ZD, Biller SA, Chodera JD, Thompson CB, Levine RL, Stein EM.

Nature. 2018 Jul;559(7712):125-129. PMID 29950729.

Here, we describe two patients with IDH2-mutant AML who had a clinical response to enasidenib followed by clinical resistance, disease progression, and a recurrent increase in circulating levels of 2HG. We show that therapeutic resistance is associated with the emergence of second-site IDH2 mutations in trans, such that the resistance mutations occurred in the IDH2 allele without the neomorphic R140Q mutation. Our observations also uncover a mechanism of acquired resistance to a targeted therapy and underscore the importance of 2HG production in the pathogenesis of IDH-mutant malignancies.

Synthetic lethal and convergent biological effects of cancer-associated spliceosomal gene mutations.

Lee SC, North K, Kim E, Jang E, Obeng E, Lu SX, Liu B, Inoue D, Yoshimi A, Ki M, Yeo M, Zhang XJ, Kim MK, Cho H, Chung YR, Taylor J, Durham BH, Kim YJ, Pastore A, Monette S, Palacino J, Seiler M, Buonamici S, Smith PG, Ebert BL, Bradley RK, Abdel-Wahab O.

Cancer Cell. 2018 Aug 13;34(2):225-241.e8. PMID 30107174.

Here, we report that although different spliceosome gene mutations impart distinct effects on RNA splicing, they are negatively selected for when co-expressed due to aberrant splicing and downregulation of regulators of hematopoietic stem cell survival and quiescence. In addition to this synthetic lethal interaction, mutations in the splicing factors SF3B1 and SRSF2 share convergent effects on aberrant splicing of mRNAs that promote nuclear factor κB signaling. These data identify shared consequences of splicing-factor mutations and the basis for their mutual exclusivity.

JAK2/IDH-mutant-driven myeloproliferative neoplasm is sensitive to combined targeted inhibition.

McKenney AS, Lau AN, Somasundara AVH, Spitzer B, Intlekofer AM, Ahn J, Shank K, Rapaport FT, Patel MA, Papalexi E, Shih AH, Chiu A, Freinkman E, Akbay EA, Steadman M, Nagaraja R, Yen K, Teruya-Feldstein J, Wong KK, Rampal R, Vander Heiden MG, Thompson CB, Levine RL.

J Clin Invest. 2018 Oct 1;128(10):4743. PMID 30222137.

Patients with the chronic blood cancer called myeloproliferative neoplasm are at a high risk for disease progression and for transformation to acute leukemia. In this paper, the authors used studies in a novel mouse model and patient samples to show that JAK2 + IDH1/2 mutations can cooperate to drive disease progression. Most importantly, they showed that combining inhibitors of JAK2 and IDH2 have increased effectiveness together, which provides the rationale for a novel clinical trial planned to open for patients with this high-risk blood cancer.

Toxicities and outcomes of 616 ibrutinib-treated patients in the United States: a real-world analysis.

Mato AR, Nabhan C, Thompson MC, Lamanna N, Brander DM, Hill B, Howlett C, Skarbnik A, Cheson BD, Zent C, Pu J, Kiselev P, Goy A, Claxton D, Isaac K, Kennard KH, Timlin C, Landsburg D, Winter A, Nasta SD, Bachow SH, Schuster SJ, Dorsey C, Svoboda J, Barr P, Ujjani CS.

Haematologica. 2018 May;103(5):874-879. PMID 29419429.

Clinical trials that led to ibrutinib's approval for the treatment of chronic lymphocytic leukemia showed that its side effects differ from those of traditional chemotherapy. Reasons for discontinuation in clinical practice have not been adequately studied. We conducted a retrospective analysis of chronic lymphocytic leukemia patients treated with ibrutinib either commercially or on clinical trials. We aimed to compare the type and frequency of toxicities reported in either setting, assess discontinuation rates, and evaluate outcomes.

ADULT BMT

Ex vivo and in vivo T cell-depleted allogeneic stem cell transplantation in patients with acute myeloid leukemia in first complete remission resulted in similar overall survival: on behalf of the ALWP of the EBMT and MSK.

Malard F, Labopin M, Cho C, Blaise D, Papadopoulos EB, Passweg J, O'Reilly R, Forcade E, Maloy M, Volin L, Castro-Malaspina H, Hicheri Y, Jakubowski AA, Orvain C, Giralt S, Mohty M, Nagler A, Perales MA.

J Hematol Oncol. 2018 Oct 20;11(1):127. doi: 10.1186/s13045-018-0668-3. PMID: 30342553.

Graft-versus-host disease (GVHD) is one of the main complications of allogeneic stem cell transplantation, a potentially curative treatment for patients with advanced blood cancers. GVHD is caused by the donor's T cells, and several strategies have been explored to reduce or eliminate T cells in patients undergoing transplant. This study compared the results of two different strategies. Patients treated at MSK had T cells removed from the donor stem cells in the laboratory by selecting the CD34+ cells, while patients in Europe received intravenous treatment with antithymocyte globulin to reduce the donor T cells. The study showed that patients in the two groups had similar long-term survival, but patients at MSK had less acute and chronic GVHD. This study was performed in collaboration with the European Society for Blood and Marrow Transplantation.

Reconstitution of the gut microbiota of antibiotic-treated patients by autologous fecal microbiota transplant.

Taur Y, Coyte K, Schluter J, Robilotti E, Figueroa C, Gjonbalaj M, Littmann ER, Ling L, Miller L, Gyaltshen Y, Fontana E, Morjaria S, Gyurkocza B, Perales MA, Castro-Malaspina H, Tamari R, Ponce D, Koehne G, Barker J, Jakubowski A, Papadopoulos E, Dahi P, Sauter C, Shaffer B, Young JW, Peled J, Meagher RC, Jenq RR, van den Brink MRM, Giralt SA, Pamer EG, Xavier JB.

Sci Transl Med. 2018 Sep 26;10(460). pii: eaap9489. doi: 10.1126/scitranslmed.aap9489. PMID: 30257956.

We have initiated a randomized, controlled clinical trial of autologous fecal microbiota transplantation (auto-FMT) versus no intervention and have analyzed the intestinal microbiota profiles of 25 allo-HSCT patients (14 who received auto-FMT treatment and 11 control patients who did not). Changes in gut microbiota diversity and composition revealed that the auto-FMT intervention boosted microbial diversity and reestablished the intestinal microbiota composition that the patient had before antibiotic treatment and allo-HSCT. These results demonstrate the potential for fecal sample banking and post-treatment remediation of a patient's gut microbiota after microbiota-depleting antibiotic treatment during allo-HSCT.

CC-486 maintenance after stem cell transplantation in patients with acute myeloid leukemia or myelodysplastic syndromes.

de Lima M, Oran B, Champlin RE, Papadopoulos EB, Giralt SA, Scott BL, William BM, Hetzer J, Laille E, Hubbell B, Skikne BS, Craddock C.

Biol Blood Marrow Transplant. 2018 Oct;24(10):2017-2024. doi: 10.1016/j.bbmt.2018.06.016. Epub 2018 Jun 20. PMID: 29933073.

Relapse is the main cause of treatment failure after allogeneic stem cell transplant (alloSCT) in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). Injectable azacitidine can improve post-transplant outcomes but presents challenges with exposure and compliance. Oral CC-486 allows extended dosing to prolong azacitidine activity. We investigated use of CC-486 maintenance therapy after alloSCT. Adults with MDS or AML in morphologic complete remission at CC-486 initiation (42 to 84 days after alloSCT) were included.

Building a CAR garage: preparing for the delivery of commercial CAR T cell products at Memorial Sloan Kettering Cancer Center.

Perica K, Curran KJ, Brentjens RJ, Giralt SA.

Biol Blood Marrow Transplant. 2018 Jun;24(6):1135-1141. doi: 10.1016/j.bbmt.2018.02.018. Epub 2018 Mar 1. Review. PMID: 29499327.

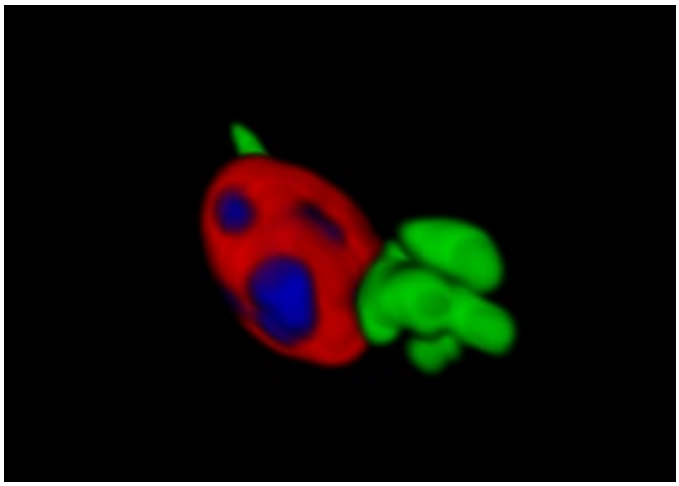
Two commercial chimeric antigen receptor (CAR) T cell therapies for CD19-expressing B cell malignancies, tisagenlecleucel (Kymriah®) and axicabtagene ciloleucel (Yescarta®), have recently been approved by the US Food and Drug Administration. The administration of CAR T cells is a complex endeavor involving cell manufacture, tracking and shipping apheresis products, and managing novel and severe toxicities. At Memorial Sloan Kettering, we have identified eight essential tasks that define the CAR T cell workflow. In this review, we discuss practical aspects of CAR T cell program development, including clinical, administrative, and regulatory challenges for successful implementation.

Allogeneic stem cell transplantation for advanced myelodysplastic syndrome: comparison of outcomes between CD34+ selected and unmodified hematopoietic stem cell transplantation.

Tamari R, Oran B, Hilden P, Maloy M, Kongtim P, Papadopoulos EB, Rondon G, Jakubowski AA, Andersson BS, Devlin SM, Ahmed S, Popat UR, Ponce D, Chen J, Sauter C, Young JW, de Lima M, Perales MA, O'Reilly RJ, Giralt SA, Champlin RE, Castro-Malaspina H.

Biol Blood Marrow Transplant. 2018 May;24(5):1079-1087. doi: 10.1016/j.bbmt.2018.01.001. Epub 2018 Jan 8. PMID: 29325829

In this retrospective analysis, outcomes of patients with MDS who had transplants with an unmodified graft at MD Anderson Cancer Center were compared to those who had transplants with a CD34+ selected graft at MSK. This analysis demonstrated similar survival among the two types of transplants but lower acute and chronic GVHD in the MSK patients, and without an increase in relapse in the patients who had transplants with a CD34+ selected graft.



This 3-D projection shows donor T cells (green) in contact with a severely damaged crypt base in the small intestine after transplantation; Paneth cells are red, and the nuclei is blue. Source: Alan Hanash lab

CD34+ cell selection versus reduced-intensity conditioning and unmodified grafts for allogeneic hematopoietic cell transplantation in patients age >50 years with acute myelogenous leukemia and myelodysplastic syndrome.

Barba P, Martino R, Zhou Q, Cho C, Castro-Malaspina H, Devlin S, Esquirol A, Giralt S, Jakubowski AA, Caballero D, Maloy M, Papadopoulos EB, Piñana JL, Fox ML, Márquez-Malaver FJ, Valcárcel D, Solano C, López-Corral L, Sierra J, Perales MA.

Biol Blood Marrow Transplant. 2018 May;24(5):964-972. doi: 10.1016/j.bbmt.2017.12.804. PMID: 29305194. Epub 2018 Jan 2.

Allogeneic stem cell transplantation is a potentially curative treatment for patients with advanced blood cancers. However, in patients over 50, physicians often prefer to use a less intense chemotherapy regimen to prepare the patients for the transplant due to other medical conditions the patient may have and concern about toxicity. This has been shown to potentially increase the risk of relapse. Investigators at MSK have developed an approach that allows using a more intense regimen in combination with T cell depletion of the donor stem cells in the laboratory by selecting the CD34+ cells. This reduces the risk of graft-versus-host disease (GVHD), one of the main complications of stem cell transplantation and eliminates the need to use toxic drugs after transplantation to prevent GVHD. This study compared the results of the two transplant strategies in patients over 50 years old with acute myelogenous leukemia and myelodysplastic syndrome who were treated at MSK. They had a lower risk of relapse and GVHD, and better survival than patients treated in a group of Spanish centers with a less intense regimen.

Acupuncture for reduction of symptom burden in multiple myeloma patients undergoing autologous hematopoietic stem cell transplantation: a randomized sham-controlled trial.

Deng G, Giralt S, Chung DJ, Landau H, Siman J, Search B, Coleton M, Vertosick E, Shapiro N, Chien C, Wang XS, Cassileth B, Mao JJ.

Support Care Cancer. 2018 Feb;26(2):657-665. doi: 10.1007/s00520-017-3881-7. PMID: 28920142. Epub 2017 Sep 17.

This study focuses on the efficacy and safety of acupuncture as an integrative medicine for managing common symptoms during hematopoietic stem cell transplantation (HCT). We observed that acupuncture was well tolerated with few attributable adverse events. True acupuncture may also prevent an escalation of symptoms, including nausea, lack of appetite, and drowsiness, experienced by patients undergoing HCT, and reduce the use of pain medications.

MYELOMA

Multiple myeloma and its precursor disease among firefighters exposed to the World Trade Center disaster.

Landgren O, Zeig-Owens R, Giricz O, Goldfarb D, Murata K, Thoren K, Ramanathan L, Hultcrantz M, Dogan A, Nwankwo G, Steidl U, Pradhan K, Hall CB, Cohen HW, Jaber N, Schwartz T, Crowley L, Crane M, Irby S, Webber MP, Verma A, Prezant DJ.

JAMA Oncol. 2018 Jun 1;4(6):821-827. doi: 10.1001/jamaoncol.2018.0509. PMID: 29710195.

This study focuses on firefighters exposed to the World Trade Center disaster, and it shows that there is evidence of excess multiple myeloma precursor disease compared to the general population. Among exposed firefighters who developed multiple myeloma, the study indicates ten to 15 years in earlier age of onset and also signs of biologically more aggressive disease.

Remission and progression-free survival in patients with newly diagnosed multiple myeloma treated with carfilzomib, lenalidomide, and dexamethasone: five-year follow-up of a phase II clinical trial.

Kazandjian D, Korde N, Mailankody S, Hill E, Figg WD, Roschewski M, Landgren O.

JAMA Oncol. 2018 Nov 21. doi: 10.1001/jamaoncol.2018.5457. Epub ahead of print. PMID: 30477009.

This publication expands on our initial results from the reported early data of a phase II study of 45 patients with NDMM and presents the long-term durability of minimal residual disease-negative complete remissions and time to progression, the last characterized by depth of response, age, and cytogenetic risk profile.

Combination therapy with carfilzomib, lenalidomide, and dexamethasone (KRd) results in an unprecedented purity of the stem cell graft in newly diagnosed patients with myeloma.

Tageja N, Korde N, Kazandjian D, Panch S, Manasanch E, Bhutani M, Kwok M, Mailankody S, Yuan C, Stetler-Stevenson M, Leitman SF, Sportes C, Landgren O.

Bone Marrow Transplant. 2018 May 4. doi: 10.1038/s41409-018-0170-0. PMID: 29728700.

This study assesses newly diagnosed multiple myeloma patients treated with KRd, focusing MRD status in both the individual patient's bone marrow and the corresponding autologous hematopoietic progenitor cell grafts during collection. Observation supports that six cycles of KRd are an efficacious and safe induction strategy prior to stem cell collection for multiple myeloma patients.

Dietary intake is associated with risk of multiple myeloma and its precursor disease.

Thordardottir M, Lindqvist EK, Lund SH, Costello R, Burton D, Steingrimsdottir L, Korde N, Mailankody S, Eiriksdottir G, Launer LJ, Gudnason V, Harris TB, Landgren O, Torfadottir JE, Kristinsson SY.

PLoS One. 2018 Nov 1;13(11):e0206047. doi: 10.1371/journal.pone.0206047. eCollection 2018. PMID: 30383820.

This publication suggests that diet might alter the risk of developing monoclonal gammopathy of undetermined significance, the precursor state of multiple myeloma (MM), and progression to MM.

CLINICAL TRIALS

These are a few of the therapeutic clinical trials in the Division of Hematologic Malignancies. For more information, visit mskcc.org/cancer-care/clinical-trials.

HEMATOLOGY

An Open Label Phase II Study of Romiplostim for Chemotherapy-Induced Thrombocytopenia.

IRB: 13-132; PI: Gerald Soff; Co-PI: Rekha Parameswaran

Chemotherapy-induced thrombocytopenia (CIT) is a frequent complication of cancer therapy. CIT typically leads to a reduction in the dose of chemotherapy that the patient can receive, with potential negative impact on cancer response. This study showed that the drug romiplostim can effectively and safely increase platelet counts in people with cancer who have CIT and allow for the resumption of chemotherapy.

Efficacy and Safety of Rivaroxaban Prophylaxis Compared with Placebo in Ambulatory People with Cancer Initiating Systemic Cancer Therapy and at High Risk for Venous Thromboembolism

IRB: 16-375; PI: Gerald Soff; Co-PIs: Rekha Parameswaran, Jodi Mones

Venous thromboembolism (VTE) is a common event in people with cancer and is associated with significant morbidity and mortality. This CASSINI study was a multinational, multi-institutional study that evaluated the prophylactic use of the anticoagulant rivaroxaban in people with cancer, who are known to be at a high risk of thrombosis. The results demonstrated a significant reduction in the relative risk of patients developing a VTE compared with placebo. Further, there was a very small and not significant increase in the risk of major bleeding. Overall, this study, as well a similar study from Canada with a different anticoagulant, will likely change practice, with high-risk patients going on prophylactic rivaroxaban to prevent VTE events, versus waiting until the patient has already experienced a thrombosis. This manuscript has been accepted by the *NEJM*.

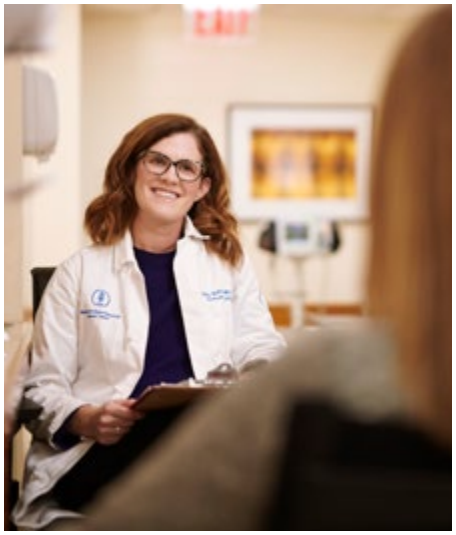
LYMPHOMA

GO39942: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase III Trial Comparing the Efficacy and Safety of Polatuzumab Vedotin in Combination with Rituximab and CHP (R-CHP) versus Rituximab and CHOP (R-CHOP) in Previously Untreated Patients with Diffuse Large B Cell Lymphoma

IRB: 18-230; PI: Matthew Matasar; Co-PI: Paul Hamlin

This randomized, double-blind, placebo-controlled phase III study will compare the efficacy, safety, and pharmacokinetics of polatuzumab vedotin plus R-CHP versus R-CHOP in participants with previously untreated diffuse large B cell lymphoma.

Hematologic oncologist Oscar Lahoud with a patient



Hematologic oncologist Kelly Bolton

Hematologic oncologist Raajit Rampal with a patient

A Phase II Clinical Trial of CPI-613 in Patients with Relapsed or Refractory Burkitt Lymphoma/Leukemia or High-Grade B Cell Lymphoma with Rearrangements of MYC and BCL2 and/or BCL6

IRB: 18-443; PI: Ariela Noy; Co-PI: Anita Kumar

The US Food and Drug Administration approved the first-in-class drug CPI-613 for relapsed/refractory Burkitt and double-hit/triple-hit lymphoma (MSK-18-443). This new drug blocks the enzymes pyruvate dehydrogenase and alpha ketoglutarate in the Krebb's cycle and has been granted Orphan drug status by the FDA. This is the first study ever dedicated to this difficult to treat disease.

A Phase II Study of Daratumumab in Patients with Relapsed or Refractory Waldenström Macroglobulinemia (WM)

IRB: 18-350; PI: Lia Palomba; Co-PI: Gottfried von Keudell

This is a multicenter phase II study designed to evaluate the efficacy of single-agent daratumumab in people with relapsed or refractory WM. The primary objective is to assess the best overall response rate (more than a 25 percent reduction in disease burden) to single-agent daratumumab in people with relapsed or refractory WM at any point in therapy.

Phase II Study of Second-Line Pembrolizumab Plus GVD for Relapsed or Refractory Hodgkin Lymphoma

IRB: 18-160; PI: Alison Moskowitz; Co-PI: Gunjan Shah

This is a multicenter phase II study evaluating pembrolizumab plus gemcitabine, vinorelbine, and liposomal doxorubicin (GVD) in transplant eligible patients with relapsed or refractory Hodgkin lymphoma following the failure of first-line multiagent chemotherapy. Patients with Hodgkin lymphoma who have failed first-line treatment and are eligible for autologous stem cell transplant will be enrolled.

Phase I/II Clinical Trial of Copanlisib and Ibrutinib in Mantle Cell Lymphoma

IRB: 18-450; PI: Connie Batlevi; Co-PI: Anas Younes

The purpose of this study is to test the safety and assess the side effects of combining copanlisib and ibrutinib. This combination of drugs could shrink mantle cell lymphoma, but it could cause side effects. Both of these drugs have been given to people before, but this is the first time that they are being given together.

LEUKEMIA

BAML-16-001-M1: A Master Protocol for Biomarker-Based Treatment of AML (The Beat AML Trial)

IRB: 17-135; PI: Eytan Stein; Co-PIs: Ross Levine, Martin Tallman

BEAT AML is a novel precision medicine trial that aims to match patients with the targeted therapy best suited for the genetic profile of their acute myeloid leukemia (AML). In the master protocol, patients' AML is rapidly genetically profiled. Based on the results of this profiling, patients are assigned to one of ten BEAT AML substudies, with additional substudies opening monthly.

MCT: A Phase II Study of the BRAF Inhibitor Vemurafenib Plus Obinutuzumab in Patients with Previously Untreated Classical Hairy Cell Leukemia

IRB: 17-135; PI: Jae Park; Co-PI: Martin Tallman

This is a multicenter, open-label, single-arm phase II trial of the oral BRAF inhibitor vemurafenib plus obinutuzumab in people with previously untreated HCL. A Simon mini-max two-stage design will be employed to assess the efficacy of the combination treatment of vemurafenib and obinutuzumab. In the first stage of the protocol, nine patients will be treated. If fewer than six CRs are seen among the first nine patients, the study will be closed for lack of efficacy. If at least seven patients respond to the treatment, then an additional 19 patients will be accrued to the second stage, for a total of 28 patients.

A Two-Part Phase I/II Study to Determine the Safety, Tolerability, Pharmacokinetics, and Activity of K0706, a Novel Tyrosine Kinase Inhibitor (TKI), in Healthy Subjects and in Subjects with Chronic Myeloid Leukemia (CML) or Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia (Ph+ ALL)

IRB: 18-229; PI: Michael Mauro; Co-PIs: Ellin Berman, Raajit Rampal

This is a phase I (first in human) trial of a novel oral tyrosine kinase inhibitor (TKI) for a Philadelphia chromosome-positive leukemia called K0706. The drug was developed to overcome highly resistant mutations, such as the T315I, as seen in both chronic and advanced leukemia. K0706 was developed by SPARC, a research branch of Sun Pharma, to offer a safer alternative to available TKIs targeting highly resistant Ph+ leukemias, where vascular and cardiovascular toxicity has been a concern.

A Phase III Study of Crenolanib or Midostaurin after Induction and Consolidation Chemotherapy for Patients with Newly Diagnosed Acute Myeloid Leukemia

IRB: 18-334; PI: Aaron Goldberg; Co-PI: Martin Tallman

The purpose of this study is to determine if giving crenolanib after chemotherapy may be more effective than giving midostaurin after chemotherapy in patients with FLT3-mutated AML. Patients will be randomly assigned to receive one drug or the other after initial chemotherapy. Both medications are taken orally (by mouth). Initial studies in patients with FLT3-mutated AML at MSK and other hospitals showed very promising results with giving crenolanib after chemotherapy, but this is the first time crenolanib has been directly compared to midostaurin.

Phase I/II Study of Pembrolizumab in Combination with TG-1101 (Ublituximab) and TGR-1202 (Umbralisib) in Patients with Relapsed-Refractory CLL or Richter's Transformation of CLL

IRB: 18-283; PI: Anthony Mato; Co-PIs: Mark Geyer, Jae Park

This study aims to determine the safety of pembrolizumab plus umbralisib and ublituximab in people with relapsed-refractory chronic lymphocytic leukemia (CLL) or Richter's transformation (RT) of CLL.

BMT

A Phase II Study of Isatuximab (SAR650984) (NSC-795145) for Patients with Previously Treated AL Amyloidosis (CIRB) (S1702)

IRB: 18-358; PI: Heather Landau; Co-PI: Hani Hassoun

This phase II trial studies how well isatuximab works in treating patients with primary amyloidosis that has come back or does not respond to treatment. Monoclonal antibodies, such as isatuximab, may interfere with the ability of cancer cells to grow and spread.

INCB 39110-119 GRAVITAS-119: A Single-Arm, Open-Label Phase I Study of Itacitinib in Combination with Calcineurin Inhibitor-Based Interventions for the Prophylaxis of Graft-Versus-Host Disease.

IRB: 18-527; PI: Miguel-Angel Perales; Co-PI: Doris Ponce

Itacitinib (INCB039110, Incyte) is a selective JAK1 inhibitor currently in clinical trials for the firstline treatment of patients with acute and chronic graft-versus-host disease (GVHD). The JAK-STAT pathway is important in inflammation and has been shown to play a critical role in GVHD, one of the main complications of allogeneic stem cell transplantation. The study is an international multicenter trial investigating the role of adding itacitinib to standard regimens to prevent GVHD.

Medical Oncologist Matthew Matasar (right) and nurse practitioner Amy Pierre

A Randomized, Open-Label Phase III Study Evaluating the Efficacy of Axicabtagene Ciloleucel Versus Standard-of-Care Therapy in Subjects with Relapsed/Refractory Diffuse Large B Cell Lymphoma (ZUMA-7) WIRB

IRB: 18-340; PI: Miguel-Angel Perales; Co-PI: Lia Palomba

The US Food and Drug Administration recently approved CD19 CAR T cells for the treatment of patients with advanced B cell lymphoma who relapse after an autologous stem cell transplant or are not eligible for the procedure. This novel approach uses the patient's immune cells to fight the tumor by inserting a gene that allows them to recognize CD19, which is present on the tumor. The current trial is a large international, multicenter trial that compares CAR T cells to autologous transplant in patients who have relapsed after the first treatment or do not respond to the initial treatment.

IIT: IL-6 Receptor Blockade to Ameliorate Acute Graft versus Host Disease and Early Toxicity after Double Unit Cord Blood Transplantation in Adults with Hematologic Malignancies

IRB: 17-616; PI: Ioannis Politikos; Co-PIs: Juliet Barker, Doris Ponce

The aim of the research in this study is to make participants' transplants safer by reducing the risk of developing GVHD and GVHD-related complications by giving participants a dose of the drug tocilizumab in addition to the standard approach for GVHD prevention. Tocilizumab reduces the risk of inflammation by blocking the effect of interleukin-6, a protein that exists in high levels in the blood when there is inflammation. Participants who receive stem cell transplants have high levels of this protein in their blood early after transplant. Therefore, the goal of this study is to reduce the risk of inflammation after transplant with the addition of tocilizumab. This could decrease the risk of developing GVHD and GVHD-associated complications.

IIT: Allogeneic Hematopoietic Cell Transplantation Using α/β+ T Lymphocyte-Depleted Grafts from HLA Mismatched Donors

IRB: 18-224; PI: Brian Shaffer; Co-PIs: Miguel-Angel Perales, Maria Cancio, Scott Avecilla

This study is being done to learn whether a new method to prevent rejection between the donor immune system and the patient's body is effective.

MCT: Phase II Trial of Intensive Chemo-Immunotherapy with Carfilzomib, Lenalidomide, Dexamethasone, and Daratumumab for Relapsed/Refractory Myeloma in the Context of Salvage Autologous Hematopoietic Cell Transplantation (the Second Chance Protocol)

IRB: 17-493; PI: Gunjan Shah; Co-PI: Sergio Giralt

The purpose of this study is to test any good and bad effects of giving a combination of study drugs before and after autologous stem cell transplant.

IIT: Allogeneic Hematopoietic Stem Cell Transplantation of an α/β+ T Lymphocyte-Depleted Grafts Conditioned with a Reduced Intensity Regimen in Patients with Myeloid Malignancies

IRB: 17-639; PI: Roni Tamari; Co-PIs: Scott Avecilla, Miguel-Angel Perales, Brian Shaffer

This is an investigator-initiated IND study introducing a new reduced intensity conditioning regimen with an alpha-beta T cell-depleted transplant. Using a reduced intensity conditioning regimen, this study aims to allow older patients and those with co-morbidities to undergo a T cell-depleted transplant, which carries a lower risk for GVHD. With the use of alpha-beta T cell depletion, the graft contains gamma-delta T cells, which are expected to improve immune recovery post-transplant.

Hematologic oncologist Audrey Hamilton with a patient

MYELOMA

Daratumumab, Carfilzomib, Lenalidomide, and Dexamethasone in Newly Diagnosed Multiple Myeloma: A Clinical and Correlative Phase II Study

IRB: 17-352; PI: Ola Landgren; Co-PI: Neha Korde

This phase II clinical trial takes advantage of the highly efficacious three-drug combination KRd, which has been developed and proven to show high rates of minimal residual disease (MRD) negativity by work from Drs. Landgren and Korde. By adding the CD38-targeted monoclonal antibody daratumumab to the KRd backbone, in the absence of bone marrow transplant, this study targets up to an 80 percent MRD negativity rate in newly diagnosed multiple myeloma patients.

Carfilzomib, Lenalidomide, and Dexamethasone in Newly Diagnosed Multiple Myeloma: A Clinical and Correlative Phase I/II Dose Escalation Study

IRB: 15-326; PI: Neha Korde; Co-PI: Ola Landgren

The purpose of this study is to test whether giving high doses of carfilzomib along with the other drugs (lenalidomide and dexamethasone) is safe and which dose is best tolerated by patients. In addition, the study is designed to test the amount of remaining myeloma cells in the body after treatment with higher carfilzomib doses, which is known as minimal residual disease.

Protocol H125001: An Open-Label Phase I/II Study of JCARH125, BCMA-Targeted Chimeric Antigen Receptor (CAR) T Cells in Subjects with Relapsed/Refractory Multiple Myeloma

IRB: 18-043; PI: Sham Mailankody; Co-PI: Craig Sauter

This is a multicenter phase I/II trial of JCARH125, a BCMA-targeted CAR T cell therapy for patients with advanced multiple myeloma. The preliminary results from the first 44 patients treated were presented at the annual ASH meeting in 2018 and showed promising efficacy with an acceptable safety profile.

C1071001: An Open-Label Phase I Study to Evaluate the Safety, Pharmacokinetic, Pharmacodynamic, and Clinical Activity of PF-06863135, a B Cell Maturation Antigen (BCMA)-CD3 Bispecific Antibody, in Patients with Relapsed/Refractory Advanced Multiple Myeloma

IRB: 17-569; PI: Alexander Lesokhin; Co-PI: Sham Mailankody

PF-06863135 is a bispecific antibody designed to bind the B cell maturation antigen protein called BCMA, which is highly expressed on multiple myeloma cells, and the T cell receptor complex protein CD3. The hypothesis of the study is that by binding both targets, PF-06863135 can bring together and activate T cells near myeloma cells and lead to myeloma cell killing. This clinical trial is a first-in-human study designed to identify a safe dose and to assess for initial signs of clinical activity by PF-06863135 in patients with advanced multiple myeloma.

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