2019
Division of Hematologic Malignancies
Annual Report

Memorial Sloan Kettering Cancer Center
The David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center is home to the largest gathering of hematologic experts ever at Memorial Sloan Kettering Cancer Center (MSK), including specialists in blood and marrow stem cell transplants, chimeric antigen receptor T cell therapy, lymphoma, leukemia, multiple myeloma, and nonmalignant blood disorders. It is highlighted on pages 36 to 41 of this report.
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We are happy to share the progress of the Division of Hematologic Malignancies at MSK over the last year. In 2019, the most noteworthy change for our Division was the opening of the David H. Koch Center for Cancer Care facility, which brings all our physicians together. In this Annual Report, we are proud to showcase details on this cutting-edge facility and interviews with Dr. Paul Hamlin (Medical Director, David H. Koch Center for Cancer Care at Memorial Sloan Kettering) and Nick Medley (Lead Guest Services Representative, David H. Koch Center for Cancer Care at Memorial Sloan Kettering).

You will find highlights for each of the Services that make up the Division, as well as the accomplishments of our nurses, advanced practice providers and pharmacists. Our team is a heterogeneous group of professionals with diverse knowledge and experience, from educating our future leaders to leading research and providing the best possible clinical care. This year we interviewed twelve members of our division, who all in their own individual way contribute to the continuing success of the Division.

Sincerely,

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

Adult Bone Marrow Transplantation

Juliet Barker  Christina Cho  David Chung

Parastoo Dahi  Arman Ghosh  Sergio Giralt

Boglarka Gyurkocza  Alan Hanash  Katharine Hsu

Ann Jakubowski  Scott James  Oscar Laboud

Heather Landau  Richard Lin  Kate Markey

Esperanza Papadopoulos  Jonathan Peled  Miguel-Angel Perales

Ioannis Politikos  Doris Ponce  Craig Sauter

Michael Scordo  Brian Shaffer  Gujan Shah

Melody Smith  Roni Tamari  Marcel van den Brink

James Young

Hematology

Simon Mantha

Jodi Mones

Rekha Parameswaran

Gerald Soff

Cy Wilkins

Hematology

Leukemia

Omar Abdel-Wahab  Elin Berman  Kelly Bolton

Renier Brentjens  Sheng Cai  Bayard Clarkson

Anthony Danyian  Andrew Dunbar  Mark Geyer

Jacob Glaas  Aaron Goldberg  Virginia Klimke

Rosa Levine  Peter Maslak  Anthony Mato

Michael Mauro  Kamal Menghirajani  Jae Park

Raajit Rampal  David Scheinberg  Alan Shih

Kytan Stein  Martin Talman  Justin Taylor

Aaron Vinay
2019 Metrics

Inpatient Visits
- Total Inpatient Visits
- Inpatient Follow-up Visits

Outpatient Visits
- Total Outpatient Visits
- Outpatient Follow-up Visits

New Outpatient Visits

Clinical Trial Accruals

Peer-Reviewed Publications

Awarded Grants and Contracts
(in millions)

Adult Bone Marrow Transplants
- Total
- Autologous
- Allogeneic
- Cords (included in Allogeneic)
Researchers Discover How T Cells Cause Post-Transplant Damage

By Jim Stallard

Graft-versus-host disease (GVHD) is a major complication of bone marrow transplantation, which is used to treat advanced blood cancers and other blood-related diseases. GVHD occurs when donor immune cells called T cells attack healthy tissues in the recipient.

One form of GVHD involves damage to the gut, or gastrointestinal tract. This can cause nausea, pain, diarrhea, and other symptoms. Researchers have shown that this damage is caused by T cells from the donor that travel to the gut, leading to impairment of the epithelial layer, which lines the surface of the organ.

What has not been clear is exactly where the T cells are attacking the intestinal tissue or which specific cells are affected. Now, Memorial Sloan Kettering researchers in the laboratory of Alan Hanash have answered that question. They have demonstrated that T cells preferentially target a site in the intestines called the stem cell compartment. The findings suggest that drugs recently approved to treat inflammatory bowel disease may be effective in treating GVHD by protecting intestinal stem cells from the donor’s immune cells.

Pinpointing the Damage Site
The epithelial layer consists of tight folds that create fingerlike projections called villi. At the base of the villi are tiny pockets called crypts. The intestinal stem cell compartment located at the base of the crypts contains two types of cells: stem cells and niche cells. Stem cells can develop into many cell types. These stem cells replenish the mature epithelial cells in the villi when they die. The niche cells help nurture and support the stem cells.

In previous research, Dr. Hanash’s lab found that stem cells in the crypts become depleted in mice with GVHD. The donor T cells are somehow responsible for this stem cell reduction. But is it a direct attack?

“We needed to find out the nature of the damage to the stem cells,” Dr. Hanash says. “Are the T cells actually targeting the stem cells themselves or do they attack the niche that supports the stem cells? Or are they really targeting the entire gut, and as a part of damaging everything, you lose some stem cells?”

Now, they have the answer: T cells go straight to the crypts and attack the stem cell compartment. This finding, published in Immunity, could help researchers find ways to block this damage following a transplant.

Visual Virtuosity
What is both impressive and critical to the success of this project is how this discovery was made — through a virtuosic feat of imaging by Ya-Yuan Fu, a researcher in the Hanash laboratory. Dr. Fu developed a way to visualize the T cells, the intestinal tissue, and its epithelial lining using an approach called 3-D microscopy.

“Normally, we get a two-dimensional image that is just a slice of what is going on in the tissue. Dr. Fu used her skills to generate these incredible high-resolution 3-D images that keep it all together and show everything.”

Alan Hanash, physician-scientist

“Tracking the location of T cells in the gut has been difficult,” Dr. Hanash says. “Normally, we get a two-dimensional image that is just a slice of what is going on in the tissue. Dr. Fu used her skills to generate these incredible high-resolution 3-D images that keep it all together and show everything.”

One surprise revealed by the imaging was how the T cells migrate to the crypt. T cells primarily use vasculature (blood vessels) to circulate and move into tissues. The vasculature is much denser in the villi, where the mature epithelial cells are. It would seem more straightforward for the T cells to migrate primarily to the villi. But that does not happen.

The reason for this appears to be a molecule called MAdCAM-1. It is present on the surface of intestinal blood vessels and was already known to play a role in attracting T cells to the intestines. Dr. Fu’s imaging experiments revealed that blood vessels expressing MAdCAM-1 are more abundant near the crypts than in the villi. This draws most of the T cells toward the crypt region.

“The data suggest that the amount of MAdCAM-1 in a certain region of tissue correlates directly with T cell invasion and with stem cell injury,” Dr. Fu says.

Protection for Stem Cells
As a final step, the researchers proved in mice that blocking the interaction between MAdCAM-1 and T cells reduces T cell invasion of the crypt and protects stem cells after bone marrow transplantation.

“Therapies that block this interaction might protect transplant patients from intestinal complications of GVHD,” Dr. Hanash says. The US Food and Drug Administration has already approved drugs like this for inflammatory bowel disease, and they are currently being tested against GVHD in clinical trials.

“Our findings reveal exactly why these drugs could be effective,” he says. “Not just by preventing T cells from getting to the gut in general but by preventing them from going to the crypts and the stem cell compartment.”
Researchers Identify a Bacterial Species That Could Protect against Hospital-Acquired Infections

By Julie Grisham

Hospital-acquired infections are a major threat, especially for people whose immune systems may be compromised because of cancer treatment. In recent years, researchers have been studying fecal microbiota transplants as a way to treat this serious complication. These transplants involve collecting stool from a healthy donor and delivering it into the intestine of the patient. The beneficial microorganisms from the transplant restore the balance of healthy bacteria in the gut.

Little is known, however, about which species of bacteria offer protection against harmful pathogens or exactly how they provide this benefit. A new study from Memorial Sloan Kettering is reporting the first evidence of a bacterial species that appears to maintain the balance of healthy microbes by killing dangerous ones. The findings also suggest how it mounts this attack. The research was reported August 21, 2019, in Nature.

“A lot of work is being done to figure out how harmful pathogens are able to colonize the human body,” says first author Sohn Kim, an MD-PhD student in the Tri-Institutional MD-PhD Program of MSK, Weill Cornell Medicine, and The Rockefeller University. “This project provides important new information about the bacteria that keep them in check.”

Focus on a Deadly Infection

The study focused on a particularly threatening hospital-acquired infection called vancomycin-resistant Enterococcus (VRE). VRE sickens about 20,000 people in the United States every year, according to the Centers for Disease Control and Prevention, and kills up to 10 percent of them. Earlier work led by former MSK graduate student Silvia Caballero, a co-author on the current study, showed that a mixture of four bacterial strains protect lab mice from VRE. These strains are normally found in the gastrointestinal tracts of healthy people.

The new study built on this earlier work by conducting a series of experiments to isolate one of these four bacterial strains: Blautia producta. “The next step was to determine the mechanism by which Blautia producta mediates protection against VRE,” Dr. Kim says. It turned out that a protein produced by Blautia producta is able to kill VRE even when the bacterial cells themselves aren’t present. Further study revealed that this protein is a lantibiotic, a type of antibiotic that is manufactured by microorganisms.

Evaluating the Effects of a Bacterial Product

The researchers did a number of additional studies. These included sequencing the gene that codes for the lantibiotic and performing RNA sequencing to determine when the gene is expressed.

They also tested the lantibiotic against about 150 strains of intestinal bacteria, to gain a sense of its spectrum of activity. This part of the research was significant because a major side effect of the antibiotics that doctors prescribe is that they can wipe out these healthy strains.

The team found that Blautia producta and the lantibiotic did not damage healthy strains. In fact, when they reviewed their library of samples collected from healthy donors, the researchers learned that about half of them already had Blautia producta and this lantibiotic product.

“It’s remarkable how precise this product is at targeting harmful microbes while sparing healthy ones,” Dr. Taur notes. “This is something we do not know how to do with any antibiotics that we have now. Our antibiotics are very clunky in comparison to the precision of what these bacteria do.”

Moving Forward with More Research

More work is needed before this approach can be tested in people with VRE infections. Drs. Kim and Taur say they haven’t even determined how a treatment would be best administered or whether they would use Blautia producta or the isolated lantibiotic. The treatment could possibly be given as a pill, or the findings from this study could be used to develop a more specialized type of fecal microbiota transplant. They plan to study various approaches in mouse models.

“Previously, studies have shown that Blautia is associated with better outcomes in people who have developed graft-versus-host disease (GVHD) after having a bone marrow transplant with donor cells,” says study co-author Marcel van den Brink, Head of MSK’s Division of Hematologic Malignancies. “In addition, we have recently found that Enterococcus is associated with increased incidence of GVHD. These findings offer exciting opportunities to control GVHD and improve outcomes for people having transplants.”

“There are a lot of things we still don’t know, but we have learned so much from this study,” Dr. Taur concludes. “It was really an amazing piece of detective work.”
Appointments, Promotions and Awards

Appointments

Arnab Ghosh
In October 2019, Arnab Ghosh joined the Adult Bone Marrow Transplant Service as Assistant Attending Physician. He received an MD from Mysore Medical College, Rajiv Gandhi University of Health Sciences, and a PhD from Hannover Medical School. Dr. Ghosh completed a residency at the Icahn School of Medicine at Mount Sinai. He also did a fellowship and postdoctoral training at Memorial Sloan Kettering. In addition to his appointment in the Adult Bone Marrow Transplant Service, Dr. Ghosh continues to work in the laboratory of Jedd Wolchok, where he is investigating potential mechanisms of resistance to immune therapies.

Kate Markey
In April 2019, Kate Markey joined the Adult Bone Marrow Transplant Service as Assistant Attending Physician. She received an MBBS and PhD from the University of Queensland and completed a residency and fellowship at the Royal Brisbane and Women's Hospital. Within Dr. Marcel van den Brink's lab, her primary research projects are focused on the complications of allogeneic marrow transplantation, particularly the relationship of the gastrointestinal microbiota with late post-transplant complications, chronic graft-versus-host disease, and the relationship between immune reconstitution and transplant outcomes. Dr. Markey provides inpatient consultation services and clinical care for patients of the Adult Bone Marrow Transplant Service.

Richard Lin
In October 2019, Richard Lin joined the Adult Bone Marrow Transplant Service as Assistant Attending Physician. He received an MD from Harvard Medical School and a PhD from the University of California in San Diego, and he completed a residency at the University of Chicago Medical Center. Dr. Lin also did a postdoctoral fellowship at the Salk Institute for Biological Studies in La Jolla, California. His fellowship was at New York University Langone Medical Center and his advanced fellowship was at Memorial Sloan Kettering. Dr. Lin focuses on caring for older people having allogeneic and autologous transplants.

Promotions

Craig Sauter
Craig Sauter was promoted to Associate Member at MSK; Associate Attending Physician in the Adult Bone Marrow Transplant Service in MSK's Department of Medicine; and Associate Professor of Medicine at Weill Cornell Medical College.

Ioannis Politikos
Ioannis Politikos was promoted to Assistant Member at MSK; Assistant Attending Physician in the Adult Bone Marrow Transplant Service in MSK's Department of Medicine; and Instructor of Medicine at Weill Cornell Medical College.

Jonathan Peled
Jonathan Peled was promoted to Assistant Member at MSK; Assistant Attending Physician in the Adult Bone Marrow Transplant Service in MSK's Department of Medicine; and Assistant Professor of Medicine at Weill Cornell Medical College.
Appointments, Promotions and Awards

Awards

Katharine Hsu received the Weill Cornell Graduate School Distinguished Alumnus Award.

Jonathan Peled received a K08 award from the NHLBI titled, “Microbiota mechanisms and biomarkers in GVHD.”

Melody Smith received a Basic Science Award from the European Society for Blood and Marrow Transplantation for her project “Intestinal Microbiome Analyses Identify Biomarkers for Patient Response to CAR T Cell Therapy.” She also received the Harold Amos Medical Faculty Development Program from the Robert Wood Johnson Foundation.

James Young received an award from the Beckman Research Institute at City of Hope and the NCI for his project “Cutaneous T Cell Lymphoma: A Paradigm for Dissecting Susceptibility and Resistance to Checkpoint Inhibition Therapy (Revision).”

Marcel van den Brink received an NCI grant for the project, “Immunobiology of Allogeneic Hematopoietic Cell Transplantation (Revision).”

Melody Smith
longitudinal, and multidisciplinary interventions to improve syndromes warrant the institution of patient-centered, preemptive, overall survival. The burden and impact of transplant-related geriatric fall are associated with potentially modifiable pretransplant geriatric syndromes of delirium or common transplant-related geriatric syndromes. The researchers was examined to establish baseline incidences and risk factors of syndromes using institutional database and electronic medical records (HCT), the incidence and impact of transplant-related geriatric syndromes in older patients with cancer. Because an increasing number of older patients undergo allogeneic hematopoietic stem cell transplantation (allo-HCT), a high incidence of enterococcal expansion was described, which was associated with graft-versus-host disease and mortality. Alto-HCT patients carrying lactose-nonabsorber genotypes showed compromised clearance of postantibiotic Enterococcus domination. Lactose is reported as a common nutrient that drives expansion of a commensal bacterium and exacerbates an intestinal and systemic inflammatory disease.

Racial Disparities in Access to HLA-Matched Unrelated Donor Transplants: A Prospective 1312-patient Analysis.

Availability of 8/8 HLA-allele matched unrelated donors (URDs) is a barrier for ethnic and racial minorities. Receipt of 8/8 HLA-allele matched URDs or either 7/8 URD or cord blood transplants was prospectively evaluated by patient ancestry from 2005 to 2017. Matched URDs were given priority if they were available. In 742 recent patients, marked racial disparity in 8/8 URD access between groups observed in earlier years persisted with only a modest increase in the percentage of 8/8 URD transplants. Increasing registry size has not resolved the racial disparity in URD access, which emphasizes the importance of alternative graft sources.

Burden and Impact of Multifactorial Geriatric Syndromes in Allogeneic Hematopoietic Cell Transplantation for Older Adults.

Multifactorial geriatric syndromes are highly prevalent in older patients with cancer. Because an increasing number of older patients undergo allogeneic hematopoietic stem cell transplantation (allo-HCT), the incidence and impact of transplant-related geriatric syndromes using institutional database and electronic medical records was examined to establish baseline incidences and risk factors of common transplant-related geriatric syndromes. The researchers discovered that transplant-related geriatric syndromes of delirium or fall are associated with potentially modifiable pretransplant geriatric risk factors, increased long-term nonrelapse mortality, and reduced overall survival. The burden and impact of transplant-related geriatric syndromes warrant the institution of patient-centered, preemptive, longitudinal, and multidisciplinary interventions to improve outcomes for older allo-HCT patients.

CD19 CAR T Cells following Autologous Transplantation in Poor-Risk Relapsed and Refractory B-cell non-Hodgkin Lymphoma.

High-dose chemotherapy and autologous stem cell transplantation (HDT-ASCT) are the standard of care for relapsed or primary refractory chemotherapy-refractory diffuse large B cell lymphoma, and only 50 percent of patients are cured with this approach. This study investigated the safety and efficacy of CD19-specific chimeric antigen receptor (CAR) T cells administered following HDT-ASCT. There was no association between CAR T cell peak expansion, persistence, or cytokine changes and progression-free survival (PFS). In contrast, 19-28z CAR T cells following HDT-ASCT were associated with a high incidence of reversible neurotoxicity and cytokine release syndrome (CRS). Following HDT-ASCT, effector CD4-positive and CD8-positive immunophenotypes may improve disease control.

Standard Antithymocyte Globulin Dosing Results in Poorer Outcomes in Overexposed Patients after Ex Vivo CD34-Positive Selected Allogeneic Hematopoietic Cell Transplantation.

Antithymocyte globulin (ATG) use mitigates the risk of graft rejection and graft-versus-host disease after allogeneic hematopoetic cell transplantation (allo-HCT), but ATG overexposure in the setting of lymphopenia negatively affects immune recovery. This study evaluated 304 patients undergoing myeloablative-conditioned ex vivo CD34-selected allo-HCT with HLA-matched donors for the treatment of hematologic malignancies. The use of weight-based ATG at a time of relative lymphopenia before ex vivo CD34-selected allo-HCT results in overdosing in heavier patients, leading to higher nonrelapse mortality (NRM) and lower disease-free survival (DFS) and overall survival (OS). Further pharmacokinetic investigation in this setting is critical to determining the optimal dosing strategy for ATG.

Selected Clinical Trials

Phase II Trial of APR-246 in Combination with Azacitidine as Maintenance Therapy for TP53-Mutated AML or MDS following Allogeneic Stem Cell Transplant
IRB: 20-030; PI: Roni Tamari; Co-PI: Virginia Klimek

In early 2020, a phase II trial of APR-246 in combination with azacitidine (Vidaza®) as maintenance therapy following allogeneic stem cell transplantation opened for accrual at Memorial Sloan Kettering. This is a multicenter study aimed at reducing the risk of disease relapse post-transplant and improving survival in patients with myelodysplastic syndrome and acute myelogenous leukemia whose disease is associated with mutated P53 gene, which is considered a very poor prognostic marker and associated with high risk of post-transplant disease relapse.
A Pilot Study of Condensed Busulfan, Melphalan, and Fludarabine Conditioning Prior to Ex Vivo CD34-Positive Selected Allogeneic Hematopoietic Cell Transplantation
IRB: 19-245; PI: Michael Scordo; Co-PIs: Valkal Bhatt, Sergio Giralt, and Roni Tamari

This pilot study led by Michael Scordo is assessing the tolerability of utilizing a novel condensed conditioning regimen — busulfan (Myleran®), melphalan (Alkeran®), fludarabine (Fludara®) — for patients with hematologic malignancies undergoing allogeneic hematopoietic cell transplantation (allo-HCT). The condensed regimen reduces the length of conditioning from eight days to five days. The primary objective is to evaluate whether the condensed regimen results in a similar proportion of patients with high-grade toxicities in the first 30 days of allo-HCT compared to historical data using the standard regimen. Secondary objectives include testing the feasibility of administering a test dose of busulfan and measuring busulfan pharmacokinetics prior to admission to calculate the daily dose of busulfan needed for the conditioning regimen. The study is ongoing.

A Phase I, Open Label, Nonrandomized, Multicenter Trial of AB-205 in Adults with Lymphoma Undergoing High-Dose Therapy and Autologous Stem Cell Transplantation
IRB: 19-165; PI: Michael Scordo; Co-PIs: Scott Avecilla and Sergio Giralt

This phase I study led by Michael Scordo assesses the safety of the investigational drug AB-205 in patients with lymphoma undergoing high-dose therapy and autologous hematopoietic cell transplantation (HDT-AHCT) to evaluate if it can reduce the side effects of this treatment approach for patients with lymphoma, but it is associated with significant side effects, including tissue injury. AB-205 is produced using endothelial cells that come from healthy human umbilical cord veins. In preclinical models, giving AB-205 after tissue injury appears to help prevent or lessen the severity and duration of side effects by more quickly healing injured endothelial cells and surrounding tissues. The study is ongoing.

INTERVIEW

Shana Strumeier
Administrative Assistant
BMT Service

As an administrative assistant, you are a key member of a clinical care team. Who are the different people you interact with day-to-day?

BMT is a unique service because we have a lot of attending physicians, I speak with many doctors both internally and externally each day. When we plan symposiums and retreats, a lot of communication goes back and forth between external continuing medical education offices and members of the Steering Committee. We plan several symposiums unique to BMT, which requires extensive communication with leading doctors all over the world. Primarily, my communication internally is with attending physicians, advanced practice providers, office coordinators, and members of management.

What do you find most challenging about your position?

I always want to make sure that everyone is happy, which is not an easy thing to do. It can be challenging to figure out how to make sure everyone in our service feels represented and heard at every level. Fortunately, the BMT Service works very cohesively together, and it’s a great team to be a part of.

How will your experiences in this role help you with your future goals and career development?

I really want to get involved in management, and I think being an administrative assistant is the perfect next step to get me there. I wasn’t always sure whether administration was for me, but this role has taught me so much. My main goal was to work with staff management and career development, and I think that being an administrative assistant has paved the way for future positions.

Who do you most look up to at work?

Is there anyone you admire and, if so, why?

There are so many people, but working as closely as I do with Sergio Giralt, Chief of the Adult BMT Service; Chelsea Brooklyn, manager; and Erika Bellet, assistant manager, those three stand out most to me. Dr. Giralt does so much for so many people, both clinically and administratively, and still manages to be the best at what he does. He is someone I look up to. I work very closely with Chelsea and Erika, and they are both great examples of how I hope to be one day. They both make sure everything in the service runs smoothly on an everyday basis. I also have learned from working with Stephanie Franco, team lead, who has taught me a lot that I will carry into my future roles at MSK.

What do you enjoy most about working at MSK?

What brought me to MSK is a sad story that ends happily. I lost my mom to cancer when I was 15, and she was treated here for melanoma. I wasn’t one of those kids who knew exactly what they wanted to do, but I knew I wanted to do something that would give back to others and help people. My cousin is a nurse at MSK, and she said the office coordinator job was open and she thought I would like it. I interviewed, and it just felt right. This is where I’m meant to be. Although, unfortunately, my mom was sick and didn’t make it, the impression that MSK left on my family and myself was so great. There wasn’t one negative experience. A lot of people are surprised by that, but it’s true. Everyone we met here was so amazing, and when I started to work here, I knew this was what I wanted to do. I want to build a career here for myself and give back to the greater purpose of why I started here.
People undergoing hematopoietic stem cell or bone marrow transplants (BMTs) face a number of unique challenges. Although many autologous transplants (those that use patients’ own cells) are now offered as outpatient procedures, the majority of allogeneic transplants (those using donor cells) are still done in the hospital setting.

These inpatient procedures entail staying in the hospital for many weeks, making the role of the inpatient nursing team especially important. As a leader in BMTs, both in the New York City area and throughout the country and the rest of the world, Memorial Sloan Kettering has unmatched expertise in managing the challenges that arise throughout the transplant process.

Mary Montefusco has spent her whole nursing career — almost a quarter of a century — at MSK. Nearly all of that time has been caring for those being treated as BMT inpatients. Ms. Montefusco began her career as a registered nurse and has been a nurse practitioner since 2007. “As an advanced practice provider (APP), I work closely with all the other members of the healthcare team,” she says. “Additionally, I develop strong relationships not only with patients but with their family members as well.”

**Developing Expertise in a Complex Setting**

APPs, a category that includes both nurse practitioners and physician assistants, have a number of responsibilities within the Adult BMT Service. They work with multidisciplinary teams to care for people having BMTs. If someone is transferred to the intensive care unit, APPs maintain close connections with patients by speaking with ICU team members. APPs are often a familiar face for patient’s families. This helps provide continuity of care. “The family members feel supported knowing that they have the same team throughout the whole process,” Ms. Montefusco says.

In the past few years, the inpatient BMT unit has also provided treatment for people receiving chimeric antigen receptor (CAR) T cell therapy. When CAR T cells grow and attack cancer cells, they release cytokine proteins. Most patients who respond to CAR T therapy develop some degree of a complication called cytokine release syndrome. Many develop neurotoxicity, too.

As a nurse practitioner, Ms. Montefusco is part of the team that helps identify and manage these neurologic effects. “Some symptoms may be decreased attention span, confusion, mental status changes, or changes in speech and handwriting,” she says. “As different symptoms occur, our team manages these symptoms and works with other consulting services, such as Infectious Diseases and Neurology, and the intensive care unit.” APPs keep patients and their families updated and supported as they undergo these therapies.

As a longstanding member of the BMT team, Ms. Montefusco is also involved in training other nurses, especially teaching them about some of the common disease processes seen in people undergoing transplants. This includes graft-versus-host disease and the different types of infections that are common after a transplant.

**Improved Well-Being for Patients, Families, and Staff**

Ms. Montefusco has also participated in research beyond the BMT Service. In 2018, she co-authored a study on the benefit of therapy dogs in the postsurgical unit at MSK. The study was led by Pam Ginex, who at the time was a nurse researcher at MSK. “I’ve always had a connection with animals and an understanding of how animals can make a difference in one’s life,” Ms. Montefusco says. “I saw that they were looking for nurses to work on this project, and I decided to get involved.”

The study looked at the quality of life in people with cancer recovering from surgery, as well as the quality of life for patients’ family members and the nursing staff. Based on comments from the study participants, the investigators learned that receiving visits from MSK’s therapy dog program, Caring Canines, improved everyone’s sense of well-being. Patients also reported having higher energy levels. “One patient said she wanted to be up out of bed sitting in a chair to meet the dog,” Ms. Montefusco says. “Another patient said the visits from the dogs gave her the motivation and energy she needed during recovery.

“At the time we did the study, Caring Canines were not yet allowed on the BMT floor,” she continues. “But after I participated in this study, I was able to obtain approval to have Caring Canines on our unit. The dogs can visit patients who are not neutropenic. Caring Canines are able to come see patients who are getting their chemotherapy before transplant and then after their blood cells have engrafted.”

She adds: “Caring Canines can really make a difference for patients. It brings a little bit of joy and a feeling of normalcy to their day. As nurses, we try to do as much as we can to help the patients feel better.”
On September 9, 2019, more than 400 people gathered to celebrate life after a blood or bone marrow transplant at Memorial Sloan Kettering’s annual Thrivers event. Now in its 24th year, the evening honors patients, caregivers, and the staff who make up MSK’s Bone Marrow Transplant (BMT) Service. These transplants can be vital treatments for people with blood cancer, such as leukemia, lymphoma, and multiple myeloma. Recovery is intensive and can involve monthlong isolation as the immune system rebuilds. Sergio Giralt, Chief of the Adult BMT Service, and Jaap-Jan “J. J.” Boelens, Chief of the Pediatric Stem Cell Transplantation and Cellular Therapies Service at MSK Kids, reported that survival rates and quality of life for transplant recipients at MSK are significantly improving, thanks to innovations at the institution, including chimeric antigen receptor T cell therapy, and outpatient care. Those advances will continue following the BMT Service’s recent expansion in the David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center in January 2020.
**Interview**

**Sonia Lebowitz**  
Care Coordinator  
Hematology Service

As a care coordinator, you are a key member of a clinical care team. Who are the different people you interact with day-to-day?

Every day is a little bit different. When I have clinic, I interact with pretty much everyone who sees the patient during that day of their visit: the pharmacist who will go over medications with the patient, the clinical research coordinator who is responsible for the protocols the patient will be on and what they will be scheduled for, and of course, the doctors, nurses, nurse practitioners, and physician assistants. Visits may last only half an hour, so it’s a big team effort to get everyone in to see a patient during that time. You get to work closely with people from very different fields.

What do you find most rewarding about your role?

Many patients come from far away and have a lot of different appointments throughout the day. They are appreciative of anything we can do to make their day easier, even if it seems small in comparison to other things that they’re going through. It makes a big difference.

Why did you want to work in hospital administration?

I used to volunteer at Camp Sunshine in Maine. We worked with children with life-threatening illnesses, and I just knew that was something I’d want to do. MSK ended up being a perfect fit, and I really love it.

What is your proudest moment at MSK?

I once had a patient come up to me who I didn’t think would remember me at all, but they said that my effort of being able to get them appointments on the same day really helped their travel itinerary. Hearing that was very rewarding.

What do you enjoy most about working at MSK?

I would say the work environment and getting to know people in different fields. You’re not just limited to people within your own circle. You get to see how the whole process comes together.

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**Selected Publications**

**Rivaroxaban for Thromboprophylaxis in High-Risk Ambulatory Patients with Cancer.**


Ambulatory patients receiving systemic cancer therapy are at varying risk for venous thromboembolism, however, the benefit of thromboprophylaxis in these patients is uncertain. In this double-blind, randomized trial involving high-risk ambulatory patients with cancer, patients without deep-vein thrombosis were randomly assigned at screening to receive ten milligrams of rivaroxaban (Xarelto®) or placebo daily for up to 180 days, with screening every eight weeks. During the intervention period, rivaroxaban led to a substantially lower incidence of such events, with a low incidence of major bleeding.

**Romiplostim Treatment of Chemotherapy-Induced Thrombocytopenia.**


Chemotherapy-induced thrombocytopenia (CIT) leads to delay or reduction in cancer treatment, and there is no approved treatment. A phase II randomized trial of romiplostim (Nplate®) was conducted versus untreated observation in patients with solid tumors with CIT. This prospective trial evaluated treatment of CIT with romiplostim. Romiplostim is effective in correcting CIT, and maintenance allows for resumption of chemotherapy without recurrence of CIT in most patients.

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**Awards**

Rekha Parameswaran received an MSK Fellowship Hematology Attending Teaching Award.
Benign Hematology Service Treats Common Blood Conditions Related to Cancer and Its Treatment

Memorial Sloan Kettering’s Hematology Service is unique among the services within the Division of Hematologic Malignancies. While the other services specialize in treating different forms of blood cancer in adults — leukemia, lymphoma, and myeloma — Benign Hematology focuses instead on blood conditions that are not cancerous. These disorders may result from cancer or its treatment, or they may be conditions that people are coping with that are unrelated to their cancer diagnosis.

The service focuses on managing problems including blood clots, thrombocytopenia (low platelet counts), low white blood cell counts, and anemia.

“We see people with all different types of cancer, as well as other non-cancerous conditions,” says Katelyn Iacocca, a physician assistant (PA) who has been with the service for almost three years. “We treat a very diverse range of patients.”

Treating a Variety of Blood Disorders

Ms. Iacocca cares for people who are being treated as inpatients. They may be hospitalized for their hematologic condition or for another problem related to their cancer. “One of the most common reasons to hospitalize a patient for a benign hematologic disorder would be a complicated or symptomatic blood clot, particularly a blood clot in the lung, called a pulmonary embolism,” she says. Blood clots are common in people with cancer. Certain chemotherapy agents can also increase the risk of blood clots, as these drugs can inflame blood vessels.

The typical symptoms of blood clots include pain or swelling in the area around the blood clot or difficulty breathing (in the case of a pulmonary embolism). However, blood clots in people with cancer are often asymptomatic and found when a person is having a scan for another purpose.

People undergoing cancer treatment may be admitted to the hospital if they have extremely low platelet counts, which puts them at a greatly increased risk of bleeding. Treatment and monitoring for low platelet counts is often done on an inpatient basis, especially in people who are already facing other complications due to cancer or its treatment.

Infections due to white blood cell counts are another frequent complication seen by members of the Benign Hematology Service.

In these cases, members of the service work closely with colleagues on the Infectious Diseases Service.

A Multidisciplinary Approach to Care

As a PA, Ms. Iacocca collaborates with the attending physicians and fellows in Benign Hematology. For as long as patients remain hospitalized, she follows up with them and their family members regularly about the management and treatment of their hematologic disorder. “Advanced practice providers, such as PAs, are designed to have a high level of direct interaction with patients and their families,” she says, “and we frequently act as a liaison between the patients and the attending physician.”

When a person is discharged from the hospital, Ms. Iacocca and the other members of the inpatient team help ensure that they continue to receive proper care and follow-up for their hematologic disorder. This may include coordinating with the patient’s existing hematologist or helping them establish care with one of MSK’s hematologists by scheduling an office visit.

A multidisciplinary approach involving the inpatient team and the outpatient nurse and office coordinator is important to ensure that patients continue to receive monitoring and tests for their condition as well as appropriate follow-up care.

“As the Benign Hematology Service continues to grow, advanced practice providers — which includes both physician assistants and nurse practitioners — are playing an increasingly important role, just as they do in many other areas of patient care at MSK.”

Katelyn Iacocca
physician assistant

““As the Benign Hematology Service continues to grow, advanced practice providers — which includes both PAs and nurse practitioners — are playing an increasingly important role, just as they do in many other areas of patient care at MSK,” Ms. Iacocca notes.
On September 3, 2019, Memorial Sloan Kettering launched the Program for Drug Development in Leukemia (PDD-L). This new program will focus on creating more phase I clinical trials for most types of leukemia in adults. Its goal is to rapidly bring novel therapies to people being treated at MSK.

We spoke to leukemia experts Eytan Stein, who will lead the new program, and Jae Park about how treatment for acute (fast-growing) leukemia has changed in the past few years. They shared their ideas on how this new program will further accelerate improvements in treating these blood cancers.

How have treatments for leukemia changed over the past few years?

**Dr. Park:** For ALL in adults, one of the big improvements is the development of new immunotherapies, including blinatumomab (Blinicyto®) and inotuzumab (Besponsa®). Blinatumomab is an antibody-based drug that works by linking T cells to leukemia cells. This enhances the T cells’ killing activity. Inotuzumab is an antibody with a drug attached, to allow the selective delivery of chemotherapy to leukemia cells. Both drugs have fewer side effects than chemotherapy. This is important because ALL is often diagnosed in older people, who may not be able to tolerate stronger drugs.

**Dr. Stein:** For AML, we have moved away from a one-size-fits-all approach, which was common for decades. As with ALL, people with AML tend to be older and therefore not strong enough for intensive chemotherapy. Now we have other options. One is a drug called venetoclax (Venclexta®), which targets a protein on leukemia cells called BCL2. The drug is given with another type of drug, called a hypomethylating agent, which affects cellular function. This combination treatment leads to remission in about 70 percent of people with AML, and those remissions tend to be long-lasting.

How has personalized medicine improved the treatment of leukemia?

**Dr. Park:** We’ve learned that about 40 percent of all cases of ALL have a genetic abnormality called the Philadelphia chromosome. This mutation is also commonly found in chronic myeloid leukemia. We’ve found that drugs that target the mutation also work for ALL, but they need to be combined with other drugs. We are now doing clinical trials to find the best combination for these drugs and are also using MSK-IMPACT™ to look for less-common mutations that can be targeted with different drugs.

**Dr. Stein:** For the 30 percent of people who don’t respond to the venetoclax combination or whose disease comes back after treatment, we have many options based on the mutations driving the cancer. For the approximately one-quarter of people who have mutations in the genes IDH2 and IDH1, the US Food and Drug Administration recently approved the drugs enasidenib (Idhifa®) and ivosidenib (Tibsovo®), respectively. We are looking at adding targeted therapies for other mutations as well. For people with secondary AML, which develops after they have been treated for myelodysplastic syndrome or another cancer, a new drug that is a formulation of two older chemotherapies together seems to be effective.

What are the roles of blood and marrow stem cell transplantation and cell therapies, like chimeric antigen receptor (CAR) T cell therapy, in treating people with acute leukemia?

**Dr. Park:** For people with high-risk ALL or those whose disease comes back after chemotherapy, bone marrow transplantation has been the only chance of a cure. More recently, a new and improved form of cell therapy called CAR T has emerged as a promising treatment to achieve a deep and complete remission even in people who have failed all standard therapies, including bone marrow transplantation. This has generated a lot of excitement in the field. MSK is leading the effort to develop effective and safe CAR T cells for people with various blood cancers. What is most exciting about this form of cell therapy is that a single infusion of T cells can result in a long-lasting remission. With continued commitment and research in the field, we are optimistic that we will improve the outcome and quality of life of people with blood cancer.
What are you most enthusiastic about?

Dr. Stein: I’m excited about all of our clinical trials, specifically the phase I trials that the PDD-L is putting forward. We hope to eventually have a trial available for every patient who doesn’t respond to standard treatment. MSK is also a founding member of the Beat AML initiative overseen by the Leukemia and Lymphoma Society. Through these efforts, we want to have a clinical trial available for every individual who doesn’t respond to standard treatment.

Dr. Park: I’m excited about all the new treatment options for all people with ALL. In the next few years, we will focus our efforts on how to best use these therapies to minimize exposure to traditional chemotherapy and shorten the duration of therapies for people with ALL, which currently last several years. We hope to achieve these goals through a series of clinical trials. We’ll use sophisticated tools to detect an extremely low level of leukemia cells, called measurable residual disease, and identify who can benefit from these new therapies.

Beyond the hematologic oncologists, who are the other members of the MSK team that contribute to the care of people with leukemia?

Dr. Stein: Our molecular pathologists and hematopathologists make it possible for us to find the genetic mutations in each patient’s cancer so that we can match them with the right therapy. This kind of testing used to take many weeks, but now they are able to get us results within a few days. It enables us to get patients on trials right away so they can start treatment almost immediately.

Dr. Park: Our nursing staff on the Leukemia Service is phenomenal, and they’re a big reason to come to MSK. They have incredible experience in managing the side effects that may come from newly approved and experimental therapies. They also understand the emotional and social needs that often come with a diagnosis of leukemia. Because of their expertise and support, we can ensure that most patients will complete their cancer treatments. Effective leukemia treatment requires strong teamwork, and we have an amazing team that I’m proud to work with every day.

Where is the PDD-L located?

Dr. Stein: People who participate in trials through the PDD-L will receive their care in the new David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center. Their treatment is provided within the Developmental Therapeutics Unit, a treatment area with a specialized cadre of nurses who have expertise in the care of people on phase I clinical trials.
Cancer is caused by gene mutations, but sometimes it’s hard to figure out which mutations actually drive tumor growth and which are just along for the ride. One way to determine this is to look for so-called mutational hot spots. These areas of the genome are mutated in tumors more frequently than would be expected by chance. The frequency suggests that they may play an active role in cancer.

MSK-IMPACT™, Memorial Sloan Kettering’s diagnostic test that looks for genetic changes in more than 400 genes in patients’ tumors, has proven quite useful in the discovery of new hot spots. Researchers in the Human Oncology and Pathogenesis Program (HOPP) have used the identification of one particular hot spot to explain why a gene called XPO1 causes cancer. The findings were published online July 8 in Cancer Discovery.

“Researchers already knew that XPO1 regulates which proteins are located in a cell’s nucleus and which get moved to the cytoplasm. This is a basic function for any cell,” says senior author Omar Abdel-Wahab, a physician-scientist in HOPP. “But until now, nobody has ever shown how the alteration of the XPO1 protein could cause cancer. This study shows how this happens.”

Decoding the Function of an Important Protein
XPO1 is often mutated in blood cancers — especially many types of lymphoma. XPO1 mutations are also found in some solid tumors. A drug that targets these mutations, called selinexor (Xpovo®), was recently approved by the US Food and Drug Administration for the treatment of multiple myeloma. It is being tested in clinical trials for other cancers at several institutions, including MSK. But researchers weren’t sure which patients were most likely to respond to the drug.

An analysis of MSK-IMPACT data led by study co-author Barry Taylor, a computational oncologist and Associate Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology, suggested that a specific mutation in XPO1, called E571, was common in cancer. To study the function of that particular mutation, Dr. Abdel-Wahab’s team put a version of the gene with the E571 mutation into mice. The mice developed cancer at a high rate. The researchers then did additional studies in the mice and in human cancer cells to find out how the mutation causes cancer.

The findings from this study could lead to a new biomarker for determining who is likely to benefit from the drug selinexor.

“We found that the mutant form of XPO1 promoted excessive cell growth,” says first author Justin Taylor, an MSK medical oncologist and member of Dr. Abdel-Wahab’s lab. “Further analysis showed that this occurs because of XPO1’s role as a gatekeeper that regulates which proteins can exit the nucleus.”

The researchers found that mutations affect the function of this gate, changing which proteins stay in the nucleus and which leave and go to the cytoplasm.

Dr. Taylor adds that the research also revealed why the drug is effective. “The mutation changes the electrical charge of the XPO1 protein, which makes selinexor bind to it more strongly. This makes the cancer cells more prone to die.”

Developing a More Personalized Approach
Clinical trials for selinexor are ongoing. Currently, MSK is participating in a trial for people with liposarcoma. The results of a trial for people with myelodysplastic syndrome were presented at a recent meeting of the American Society of Hematology.

Dr. Abdel-Wahab says that the E571K mutation may prove to be an effective way to determine who is likely to benefit from selinexor. This could influence future clinical trials of the drug and lead to a more personalized approach to who gets the drug.

The researchers also plan to study the role of other XPO1 defects in cancer, including cases where the gene is overexpressed but not necessarily mutated.
Appointments, Promotions and Awards

Promotions

Justin Taylor
Justin Taylor was promoted to Assistant Member at MSK; Assistant Attending Physician in the Leukemia Service in MSK’s Department of Medicine; and Instructor in Medicine at Weill Cornell Medical College.

Jae Park
Jae Park was promoted to Associate Member at MSK; Associate Attending Physician in the Leukemia Service in MSK’s Department of Medicine; and Associate Professor of Medicine at Weill Cornell Medical College.

Kelly Bolton
Kelly Bolton was promoted to Assistant Member at MSK; Assistant Attending Physician in the Leukemia Service in MSK’s Department of Medicine; and Instructor in Medicine at Weill Cornell Medical College.

Awards

Omar Abdel-Wahab received the following awards in 2019:
- Award from Indiana University and the Leukemia and Lymphoma Society (LLS) for his project “Development of Therapeutic Strategy for the Treatment of MDS”
- Awards from the LLS and the Weizmann Institute of Science’s Rising Tide Foundation for his project “Early Diagnosis and Treatment of Preleukemia”
- Award from the National Cancer Institute (NCI) with co-PIs Ari Melnick of Weill Cornell Medicine and Adolfo Ferrando of Columbia University for their project “ECOG-ACRIN Integrated Leukemia Translational Science Center (LTSC)”

Kelly Bolton received a K08 award from the NCI for her project “Impact of Oncologic Therapy on Clonal Hematopoiesis and Subsequent Risk of Therapy-Related Leukemia.”

Andrew Dunbar received a Physician-Scientist Training Award from the Damon Runyon Cancer Research Foundation.

Jacob Glass received a K08 award from the NCI for his project “Lineage Identification and Targeted Therapeutics in Acute Leukemia (Revision).”

Lindsey Roeker received an award from the American Society of Hematology for her project “Checkpoint Inhibition with PI3K Inhibitor and Anti-CD20 Antibody for CLL and Richter’s Transformation.”

Martin Tallman marked the following achievements:
- Robert A. Kyle Lifetime Achievement Award for Outstanding Clinical Scientist in Hematology and Oncology from the Mayo Clinic
- Incumbent of the Cassidy Family Endowed Faculty Chair
- Vice President of the American Society of Hematology
- Award from the NCI with Co-PIs Carol Aghajanian, Michael Morris, Nancy Lee, and Oliver Zivanovic for their project “Network Lead Academic Participating Site: Memorial Sloan Kettering Cancer Center”

Justin Taylor was awarded the Harold Amos Medical Faculty Development Program from the Robert Wood Johnson Foundation.
Approximately 8 to 19 percent of patients with acute myeloid leukemia (AML) have isocitrate dehydrogenase-2 (IDH2) mutations, which occur at active site arginine residues R140 and R172. This first-in-human phase I/II study evaluated enasidenib (Idhifa®, Idhifa®) doses of 50 to 650 milligrams per day, administered in continuous 28-day cycles, in patients with mutant IDH2 hematologic malignancies. Among all 345 patients, the most common grade 3 or 4 treatment-related adverse events were hyperbilirubinemia (10 percent), thrombocytopenia (7 percent), and IDH differentiation syndrome (6 percent). Enasidenib was well tolerated and induced molecular remissions and hematologic responses in patients with AML for whom prior treatments had failed.

Activating Mutations in CSF1R and Additional Receptor Tyrosine Kinases in Histiocytic Neoplasms.

Histiocytoses are clonal hematopoietic disorders frequently driven by mutations mapping to the BRAF and MEK1 and MEK2 kinases. Currently, however, the developmental origins of histiocytoses in patients are not well understood, and clinically meaningful therapeutic targets outside of BRAF and MEK are undefined. In this study, activating mutations were uncovered in CSF1R as well as rearrangements in RET and ALK that conferred dramatic responses to selective inhibition of RET using selpercatinib and crizotinib (Xalkori®), respectively, in patients with histiocytosis.

Asciminib in Chronic Myeloid Leukemia after ABL Kinase Inhibitor Failure.

Asciminib is an allosteric inhibitor that binds a myristoyl site of the BCR-ABL1 protein, locking BCR-ABL1 into an inactive conformation through a mechanism distinct from those for all other ABL kinase inhibitors. In this phase I study, the primary objective was to determine asciminib’s maximum tolerated dose, the recommended dose, or both. Asciminib was active in heavily pretreated patients with Chronic Myeloid Leukemia (CML) who had resistance to or unacceptable side effects from tyrosine kinase inhibitors (TKIs), including patients in whom ponatinib (Iclusig®) had failed and those with a T315I mutation.

Toxicity and Response After CD19-Specific CAR T-Cell Therapy in Pediatric/Young Adult Relapsed/Refractory B-ALL.

Chimeric antigen receptor (CAR) T cells have demonstrated clinical benefit in patients with relapsed/refractory B cell acute lymphoblastic leukemia (R/R B-ALL). This multicenter clinical trial was undertaken to determine toxicity, feasibility, and response for this therapy. The data support the safety of CD19-specific CAR T cell therapy for R/R B-ALL and also suggest that the dose intensity of conditioning chemotherapy and minimal pretreatment disease burden have a positive impact on response without a negative effect on toxicity.

Selected Clinical Trials

A Phase I/II Study of Oral LOXO-305 in Patients with Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma or Non-Hodgkin Lymphoma.
IRB: 19-077; PI: Anthony Mato; Co-PIs: Justin Taylor and Andrew Zelenetz

Anthony Mato is leading the development of LOXO 305 at Memorial Sloan Kettering. This agent is a first-in-class noncovalent BTK inhibitor being tested in patients with chronic lymphocytic leukemia and B cell non-Hodgkin’s lymphoma. The drug is unique in that it is designed to overcome resistance mutations in the BTK gene, which can occur when patients are treated with covalent BTK inhibitors, including brutinib (Imbruvica®). MSK was the highest accruing site for this study internationally. Dr. Mato presented the data as an oral presentation at the 2019 annual meeting of the American Society of Hematology. A manuscript for this study is currently under development.
A Phase I/II, Open-label, Dose-Escalation and Dose-Expansion Cohort Study of SNDX-5613 in Patients with Relapsed/Refractory Leukemias, Including Those Harboring an MLL/KMT2A Gene Rearrangement or Nucleophosmin 1 (NPM1) Mutation
IRB: 19-448; PI: Eytan Stein; Co-PI: Martin Tallman

MLL rearrangements are common in patients who have acute leukemia that arose as a result of receiving prior chemotherapy, a patient population that we see commonly at Memorial Sloan Kettering. Researchers have identified a protein called menin as a crucial link between having an MLL rearrangement and developing leukemia. In laboratory models of acute leukemia, blocking menin leads to disease regression. Eytan Stein is leading a phase I/II study of SNDX-5613, a novel menin inhibitor, in patients with relapsed and refractory acute leukemia that harbors an MLL rearrangement or NPM1 mutation. Early results of this exciting clinical trial are expected to be reported within the next year.

A Phase II Study of IL-1 Receptor Antagonist Anakinra to Prevent Severe Neurotoxicity and Cytokine Release Syndrome in Patients Receiving CD19-Specific Chimeric Antigen Receptor T Cells
IRB: 19-168; PI: Jae Park; Co-PIs: Bianca Santomasso and Craig Sauter

This phase II clinical trial is designed to investigate the efficacy of the IL-1 receptor antagonist anakinra (Kineret®) to prevent or reduce severe side effects associated with CD19 chimeric antigen receptor (CAR) T cells, particularly cytokine release syndrome and neurotoxicity. The study is ongoing and, if successful, will increase the safety of CD19 CAR therapy while preserving its therapeutic potency, so it can become widely available and outpatient friendly.
Memorial Sloan Kettering hematologic oncologist Ellin Berman is grateful for all the opportunities she’s had throughout her decades-long career at MSK. Because of that, she believes it’s important to pay those opportunities forward toward future generations of physicians and scientists.

Nine years ago, Dr. Berman reached out to the University of Chicago, which she attended as an undergraduate, about setting up a summer program at MSK for students interested in science and medicine. She worked with the dean and administrators there to establish a way for interested students to apply to come during their summer vacations. Since then, applications for the MSK summer science program have grown each year.

“When I was an undergraduate, it was challenging to find science-related work over the summer,” explains Dr. Berman. “After I became an attending here at MSK, I wanted to make it easier for students behind me to take part in high-level laboratory work, as well as to gain clinical experience in a busy hospital.”

**A Range of Activities**

Through the University of Chicago’s Jeff Metcalf Internship Program, students receive a stipend that covers their expenses. Between two and four students participate in the program at MSK each year. “The University of Chicago opened the door for me,” Dr. Berman says, “and now I want to do the same for the next generation.”

Students spending the summer at MSK through the program have the opportunity to work in a leukemia research lab within the Sloan Kettering Institute or the Human Oncology and Pathogenesis Program. They are usually assigned a specific project, under the guidance of a postdoc in the lab.

“Many of our basic scientists really enjoy the opportunity to host a college student for the summer because they want to open up the science experience for college students, too,” Dr. Berman notes. In addition to their lab work, each student spends time in the leukemia clinic with Dr. Berman. They also have the opportunity to attend clinical and scientific conferences and to round with the inpatient Leukemia Service.

“Many of the students who have gone through the program have later been accepted at top-level medical schools or MD-PhD programs,” Dr. Berman says, including at least one who enrolled at Weill Cornell Medicine, across the street from MSK.

**A Rewarding Program for All Participants**

“The summer program is rewarding both ways,” Dr. Berman notes. “For me, it’s about the positive feelings I get when I link back to the University of Chicago and meet all these really interesting students from around the country. But it’s also about having the students see how leukemia care is delivered in the outpatient and inpatient settings here.”

“These internships are rare gems of opportunity that can make a world of difference in someone’s future career,” according to one student who recently participated. “I have learned so much more than I could possibly imagine about cancer while working at MSK in New York, and it has made me consider a possible future in oncology, helping cancer patients.”

“The opportunity to perform research at a highly translational research institution was eye-opening,” says another recent participant. “To perform research on patient samples, then to witness research being translated from the lab to the clinic, has influenced me to pursue a research-oriented specialty in medicine. The most exciting part of medicine, to me, is the discovery of scientific knowledge and the ability for the newfound knowledge to change the clinical setting.”

**The Power of Collaboration**

Throughout her career, Dr. Berman has been a leader in developing and leading clinical trials for different types of leukemia. She has made a number of contributions in the field of leukemia research, including developing therapies that are personalized and more targeted. She is currently involved in research looking at some of the side effects of tyrosine kinase inhibitors, such as imatinib (Gleevec®), especially their effects on bones.

“One of the real strengths of this institution is that it gives you the opportunity to follow a problem to its root,” Dr. Berman concludes. “There’s a certain momentum that’s gained when you have many people looking at the same topic. If you have an idea, you can always find someone who is looking at the same problem, usually in a different way, and find the right people to support it.”

Dr. Berman credits Marcel van den Brink for making that possible. “That’s when real advances are made,” she says.
The increased use of targeted therapies and immunotherapies has changed the course of treatment for many people with leukemia. These classes of drugs work very differently from chemotherapy but still have a range of potentially serious toxicities.

As a leader in developing clinical trials to investigate drugs for blood cancer, the Division of Hematologic Malignancies at Memorial Sloan Kettering has a great deal of experience in recognizing and treating these side effects. One drug that’s been a recent focus of research is blinatumomab (Blincyto®), which is in a class of antibody drugs called bispecific T cell engagers (BITEs).

At the annual meeting of the American Society of Hematology (ASH) in December 2019, MSK investigators presented a poster that reported data on the use of blinatumomab in patients and the management of side effects from this drug. “Blinatumomab is very expensive, and it’s labor-intensive to give to patients,” says clinical pharmacy specialist Amber King, the poster’s first author. “Because MSK uses the drug quite often, we’re in a unique position to describe how we give it and how we manage patients.”

A Promising Type of Immunotherapy

Blinatumomab was approved in 2014 for the treatment of B cell acute lymphoblastic leukemia (ALL) in people who don’t respond to other therapies. B cell ALL arises when white blood cells called B cells begin growing out of control. Cancerous B cells replace healthy B cells in the bone marrow, increasing the susceptibility to infections and also leading to other symptoms.

The mechanism by which blinatumomab and other BITEs go after cancer cells is unique. The drugs, which are considered a type of immunotherapy, work in a similar way to chimeric antigen receptor (CAR) T therapy: They reprogram a patient’s immune system — specifically the T cells — to attack cancer cells. The difference is that instead of being customized for each person, like CAR T therapy is, BITEs provide a more off-the-shelf way of bringing together cancer-killing T cells and cancerous B cells.

One of the potentially serious toxicities caused by blinatumomab is cytokine release syndrome (CRS). “This condition is characterized by profound inflammation,” Dr. King says. “It can lead to fevers, low blood pressure, and organ dysfunction.”

The other potentially serious side effect is neurologic toxicity. This can range from difficulties speaking and remembering certain words to much more serious problems, like seizures.

“Because this drug is so effective at finding the bad leukemia cells, it has great potential to overwhelm the immune system,” Dr. King explains. “It tends to have less dramatic effects than CAR T therapy, but the side effect profile is very similar.”

Using Data to Guide Future Treatments

In the ASH poster, Dr. King and her colleagues reviewed the medical records of 62 adults who received blinatumomab at MSK. They analyzed which side effects were most common, how severe those side effects were, and how they were treated.

Overall, they found that certain biomarkers, especially an increase in blood levels of interleukin-6 and the levels of certain proteins and other chemicals (called acute phase reactants) may indicate which people are most likely to experience severe toxicity. They also reported that changing how blinatumomab is administered may help alleviate some of these side effects.

“This drug is given as a continuous infusion, and one of the things we found is that turning the infusion off can help resolve these toxicities, including CRS and neurologic problems,” Dr. King says. “We also found that certain drugs, including the steroid dexamethasone, can help reduce side effects, especially when they are given earlier in the course of treatment.”

She adds that other centers may be hesitant to use blinatumomab, in part because of the concern about managing toxicities, and that one of the goals of this research at MSK is to provide guidance to other hospitals. “As a clinical pharmacist, one of my main roles is to ensure that drugs are being utilized safely and appropriately based on available evidence.”

A Promising Type of Immunotherapy

“As a clinical pharmacist, one of my main roles is to ensure that drugs are being utilized safely and appropriately based on available evidence.”

Amber King
clinical pharmacy specialist

Amber King
Dr. Seema Gupta Endowed Visiting Professor and Lectureship

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 a fellowship in hematology/oncology at Memorial Sloan Kettering and served as an attending physician in the Leukemia and Lymphoma Service from 2001 to 2005. Dr. Gupta suffered a brain injury and subsequently passed away.

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. The visiting professor and lectureship fund in her name supports the visit of a world-renowned leukemia expert to MSK each year. The inaugural Dr. Seema Gupta Symposium was held on Friday, September 27, 2019. Mark Levis of Johns Hopkins University served as the keynote speaker. Maximilian Stahl, Scott Millman, and Brian Ball, fellows in MSK’s Leukemia Service, gave presentations on their current research. Vishal Gupta, a cousin of Dr. Gupta, attended the event. The next Dr. Seema Gupta Symposium will take place Friday, September 4, 2020.

INTERVIEW

Giovanney Mendoza
Office Coordinator
Leukemia Service

What do you find most rewarding about your role?
Sometimes patients ask us to push things earlier to accommodate a family function, like a graduation or a wedding. When we’re able to do that and let them be present in aspects of their lives other than their medical care, that’s very rewarding.

What is the most exciting thing you’re working on right now?
Eytan Stein, a hematologic oncologist, has let me sit in on meetings to work on how we provide care to patients in underserved communities. It’s often harder for these patients to afford not just the medical care here but the costs that surround it. This initiative requires working with different medical services, Social Work, and Patient Financial Services to find ways we can enhance care for those patients. Sitting in on those meetings has been eye-opening, and I’ve been lucky to do that.

How will your experiences in this role help you with your future goals and career development?
It has made me a lot more empathetic toward the patients that I work with. I want to pursue a career in social work, and a lot of that is direct patient care and working with patients to find ways to help them get through their circumstances. I think this role is preparing me for that and helping me understand what patients are asking and how I can do my best to provide it. Or if I can’t, I can connect them to resources that can help.

Who do you most look up to at work? Is there anyone you admire and, if so, why?
I would say it has to be the three people on my clinical team. Some people may feel that their doctor is minimally involved in their care, but Dr. Stein really gives so much attention to all the patients that he sees. Coleen Ranaghan, our nurse practitioner, and Alexandra Napolitano, our nurse, do the exact same thing. It has been really inspiring to watch the way they work in their practices, dedicate so much time, have so much empathy, and make sure we can do all we can for our patients and fight for them every single day. When I become a clinician in the future, I hope to apply the same style that they do.

What do you enjoy most about working at MSK?
I enjoy the people I work with every day, not just the clinical team but also the other office coordinators I work with. Everyone is such a great team member and tries to push each other to be better every day. It is a very supportive group, which is not something you can always find.
Peripheral T cell lymphoma (PTCL) is a rare, aggressive type of non-Hodgkin lymphoma. In November 2018, treatment for this blood cancer took a major step forward when the US Food and Drug Administration approved a combination therapy for people newly diagnosed with the disease.

The combination therapy involves adding a drug called brentuximab vedotin (Adcetris®) to chemotherapy. In the phase III clinical trial that led to the approval, the treatment combination more than doubled the time in which the disease didn’t worsen and also helped people with PTCL live longer.

We spoke with Memorial Sloan Kettering medical oncologist Steven Horwitz, who played a leading role in the trial, about what went into this research and what it means for people with PTCL.

How will this new approval change the treatment of PTCL?
For two decades, there has been little change in treatment for people newly diagnosed with PTCL. The standard therapy has been a chemotherapy combination known as CHOP, which is named after the drugs in the mixture. Doctors had tried an intensified variation of that regimen, but it didn’t produce any clear-cut improvement in long-term effectiveness.

That’s what makes the results from this trial so striking. Adding brentuximab vedotin to standard chemotherapy made a huge difference in progression-free survival, which is how long a person lives without the cancer growing. In people who received the combination, progression-free survival was a median of 48 months. In those who received only CHOP, it was 21 months. There was also an increase in overall survival. More people who received the brentuximab vedotin combination were alive after three years.

What does brentuximab vedotin do?
The drug is a monoclonal antibody that targets a protein, CD30, found on some cancer cells. It is already approved for treating Hodgkin lymphoma. The clinical trial tested its effectiveness in people whose PTCL cells expressed CD30. The side effects included nerve damage, nausea, and diarrhea. They were not too severe for most people and are similar to the side effects of CHOP and other chemotherapy regimens.

What was MSK’s role in the clinical testing of this combination?
MSK played a big role in the background research, including helping lead a study several years ago that looked at brentuximab vedotin for the treatment of other T cell lymphomas. Those results gave us the rationale to do this big phase III trial, called ECHELON-2, testing it in people with PTCL. The trial involved more than 400 people. MSK enrolled more patients than any other institution in the trial, both at Memorial Hospital and at MSK Commack on Long Island. We reported the results of the trial in December 2019 at the annual meeting of the American Society of Hematology and in The Lancet soon after. So MSK played a leading role, but it was truly a worldwide effort. More than 140 institutions enrolled patients.

When did you realize this new treatment approach was helping patients?
It was a double-blind study. That means neither the doctors nor patients knew which treatment was being given to a specific person in the trial. In late September 2018, I flew out to Seattle to look at the data when it was finally unblinded. Seattle Genetics, the company that makes brentuximab vedotin and sponsored the trial, was hosting researchers to analyze the data and start writing up the results. I got there late on a Friday night, and it was not until then that I learned that adding brentuximab vedotin not only improved progression-free survival but also overall survival. The improvement in overall survival was the big surprise — it was a dramatic benefit we were not expecting and that had never before been shown in a frontline study of T cell lymphoma.

The results were so conclusive and of immediate importance to doctors and patients that it led to one of the fastest ever FDA approvals. It was about six weeks from when the trial data were revealed to approval on November 16, 2019. The combination approach using brentuximab vedotin is now available to all newly diagnosed adults with a PTCL subtype called anaplastic large cell lymphoma, which is characterized by CD30 expression. It is also approved for people who have any other CD30-expressing PTCL.

What’s next for this research?
We are taking a closer look at the data to get a better understanding of which people with CD30-positive cancer will do well with the brentuximab vedotin combination and who might need additional therapy.

We don’t have evidence that people whose lymphoma is CD30-negative will benefit from this treatment. But our lymphoma research program is looking at identifying people who can benefit from other targeted therapies. Our T cell lymphoma group is particularly focused on using our increased understanding of the biology of T cell lymphoma to identify more-targeted and hopefully more-effective therapies. This trial result is a good proof of principle for what we’re trying to do, which is develop more individualized and potent therapies for specific lymphoma subtypes.
I grew up in the suburbs of Annapolis, Maryland. My dad worked for the Small Business Administration, which is part of the federal government. My mom was a high school science teacher, and she encouraged my early interest in science. One fond memory is how my brothers and I would assemble large and elaborate insect collections every summer.

Growing up, I originally wanted to be an architect. I also really liked art and the humanities. I’m not sure what first got me into medicine. I think it was probably curiosity about how the immune system can fight off infections and infectious diseases.

When I went to college, at the University of Maryland, Baltimore County, I majored in biochemistry, with a premed focus, and minored in Spanish. Entering college, I probably had a stronger background in English and history than I did in science. But when I started to do college-level biochemistry, I just fell in love with it. I loved the courses and the clarity of the problems.

I decided to do my PhD in immunology at the University of Pennsylvania. That’s when I found out about MD/PhD programs. That trajectory appealed to me: being able to have a bigger impact, on a broader scale, by doing research that could change the way that medicine is done.

I joined the lab of Steve Reiner. He was an architect. I also really liked art and the humanities. I’m not sure what first got me into medicine. I think it was probably curiosity about how the immune system can fight off infections and infectious diseases.

At that time, Craig Thompson was also at Penn, and I was hearing a lot about his research. I became more and more interested in metabolism. I considered staying at Penn to do a postdoc with him, but for a variety of reasons, my wife and I wanted to be in New York City.

Then when I was in residency, I found out that Dr. Thompson was becoming President of MSK. That’s when I knew that I had to do my postdoc with him.

A New Role for an Old Player
It was right around then that the IDH mutations were discovered. Dr. Thompson and others had figured out that the mutations make a metabolite that can disrupt the decisions that stem cells make and cause cancer. That was just fascinating to me — that a tiny five-carbon metabolite could completely change a cell’s fate. When the IDH mutations were discovered, no one thought these boring housekeeping genes could be cancer drivers. I came into the lab wanting to attack metabolism from that angle: How do these metabolites affect the decisions that cells make?

When I was trying to figure out what my project would be as a postdoc, a couple of things intrigued me. One was the fact that this metabolite, 2HG, is not really one metabolite. It’s actually two different ones — they’re enantiomers [mirror images] of each other. The cancer-associated mutations make one of the mirror images, called the D enantiomer. When people were trying to figure out what the D enantiomer did, they were using the other enantiomer, called L, as a control. Unexpectedly, they found that the L enantiomer is much more potent. No one knew what to make of this. But because cancers don’t make the L enantiomer, people didn’t seem that interested in finding out.

The other thing that I found fascinating was that there are waste disposal enzymes for both of those metabolites. They’re enantiomer-specific and conserved throughout evolution. Kids born with deficiencies in either of those waste disposal enzymes suffer from severe developmental pathologies, neurologic devastation early, and an early death. But the kids missing the L disposal enzyme also get brain tumors. So that told me that normal cells must be making the L form. I decided to figure out where this metabolite is coming from and what it does to cells.

What we found is that putting any cell into a low-oxygen environment, called hypoxia, makes it produce the L form. This stronger form causes cells to acquire features of stem cells, or stemness. This was intriguing because it’s been known for decades that stem cells reside in and depend on hypoxic niches in the body. And we knew that the phenotype of that IDH mutant was a stem cell phenotype. So we asked: Could this be an endogenous stemness program that the IDH mutations are mimicking? That’s what my lab is trying to figure out — what these two forms of 2HG are doing and how they can be manipulated to treat cancer or enhance stem cell function.

Physician-scientist Andrew Intlekofer studies the relationship between metabolism and cell differentiation. He came to Memorial Sloan Kettering in 2011 as an oncology fellow and now has his own lab in the Human Oncology and Pathogenesis Program.
**Approach to Science**
I think I take after Dr. Thompson a little bit in the way I approach science. I like the big ideas. I like people to always ask why, why, why, and really try to tackle the important questions.

That doesn’t mean experiments have to be supertechnical. In fact, I’m always asking myself: What is the simplest possible experiment I can do to answer this question? What is something that anyone could do that will answer yes or no to this hypothesis? I think papers are getting too bloated in terms of the data requirements.

In my lab, I try to foster a collegial, collaborative environment where people feel comfortable asking questions. No question is dumb. I like it when people are interacting and helping one another. I like teamwork. I like an informal atmosphere, but I like people to be thinking deeply about the questions and trying to understand why this is an important question. If you can’t figure out why it’s an important question, you should not be doing it.

I also want my lab to span the gamut of science, from doing basic biochemistry with pure enzymes and substrates in vitro, to cell lines, to mouse models and human specimens. I want people to do the full range of bench to bedside research, to be able to make a discovery in a patient but then go deep into a molecular mechanism. And vice versa: I want them to start with the biochemistry and then get it into a question that could be relevant to patients.

One of the great things about being at Memorial Sloan Kettering is you can do work that you just can’t do anywhere else in terms of translational research. The most advanced, newest drugs are being tested here and nowhere else.

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**Interview**

**Veenna Minnal**
Clinical Research Specialist
Lymphoma Service

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**Why did you want to work in clinical research?**
I did research in economics before, which is very different from working at MSK. But I really think it’s rewarding to be able to interact with patients, learn more about them, and learn more about cancer and hematologic malignancies.

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**What is the most exciting thing you’re working on right now?**
We’re working on compiling a list of metrics for screening patients. Being able to present that to the physicians and see how our screening helps get patients into clinical trials is really rewarding at the end of the day.

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**How will your experiences in this role help you with your future goals and career development?**
I want to be a dentist, which is different, but I really think that having interactions with patients and working with a bunch of different people on different career paths is something that will help me in the future.

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**Who do you most look up to at work? Is there anyone you admire and, if so, why?**
I really admire my manager, Rhea Boxill. She deals with so many different people daily, but she’s always willing to lend us a hand and make time for us to talk to her. If we have any problems during the day, she’s always willing to listen and help us problem solve.

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**What do you enjoy most about working at MSK?**
I like being able to work with so many different people from different areas and working with such a supportive institution. There’s always help if you ask for it, and everyone is willing to lend a hand.
Appointments, Promotions and Awards

Appointments

Lorenzo Falchi
In October 2019, Lorenzo Falchi joined the Lymphoma Service as Assistant Attending Physician. He received an MD from the University of Perugia and completed a residency in medicine at the Yale School of Medicine. Dr. Falchi also did a hematology oncology fellowship at NewYork-Presbyterian Hospital/Columbia University Irving Medical Center. Dr. Falchi cares for people with all types of Hodgkin and non-Hodgkin lymphoma.

Anita Kumar
Anita Kumar was promoted to Assistant Member at MSK; Assistant Attending Physician in the Lymphoma Service in MSK’s Department of Medicine; and Assistant Professor of Medicine at Weill Cornell Medical College.

Colette Owens
Colette Owens was promoted to Assistant Clinical Member at MSK and Assistant Attending Physician in the Lymphoma Service in MSK’s Department of Medicine.

Promotions

Matthew Matasar
Matthew Matasar was promoted to Associate Member at MSK; Associate Attending Physician in the Lymphoma Service in MSK’s Department of Medicine; and Associate Professor of Medicine at Weill Cornell Medical College.

Awards

Steven Horwitz’s project, “Informed combination strategies for peripheral T-cell lymphomas” was funded by the NIH.

Andrew Intlekofer received a Steven A. Greenberg Startup Grant for his project “Metabolic and Epigenetic Regulation of T-Cell Differentiation and Lymphomagenesis.”

Alison Moskowitz received an award from the LLS and a Steven A. Greenberg Startup Grant for her project “JAK/STAT Inhibition as a Therapeutic Strategy in T Cell Lymphoma.”

Ariela Noy received an award from the University of California in Los Angeles and the NCI for her project “AIDS Malignancy Consortium (Supplement).”

Santosh Vardhana received a Burroughs Wellcome Fund Career Award for Medical Scientists. He also received grant funding for his research project “Investigating Metabolic Susceptibilities of Exhausted T Cells.”

Anas Younes received a Distinguished Leadership Award from the Lymphoma Research Foundation (LRF) to honor his accomplishments as a lymphoma researcher and physician, his contributions to the lymphoma community, and his support for the LRF. Dr. Younes accepted the award at the LRF’s annual gala in New York on September 26.
Publications and Clinical Trials

Selected Publications

Metabolic Signatures of Cancer Cells and Stem Cells.
Intlekofer AM, Finley LWS. Nat Metab. 2019;1(2):177-188. doi:10.1038/s42255-019-0032-0.

This paper discusses the metabolic programs that support proliferation and explores how metabolic states are intimately intertwined with the cell fate decisions that characterize stem cells and cancer cells. By comparing the metabolism of pluripotent stem cells and cancer cells, these researchers hope to illuminate common metabolic strategies as well as distinct metabolic features that may represent specialized adaptations to unique cellular demands.

Genomic Profiling of Mantle Cell Lymphoma Suggests Poor-Risk Profile Is Present at Diagnosis and Does Not Arise by Tumor Evolution.

Despite major clinical advancements, mantle cell lymphoma (MCL) remains a therapeutic challenge, with a considerable number of patients experiencing a dismal course. This study sought to map the genomic landscape of MCL at diagnosis and at disease progression. Researchers in this study aimed to identify the genomic drivers of an aggressive phenotype, resistance, and relapse, and to characterize the genomic evolution of this disease.


Based on the encouraging activity and manageable safety profile observed in a phase I study, the ECHELON-2 trial was initiated to compare the efficacy and safety of brentuximab vedotin (Adcetris®), cyclophosphamide (Cytoxan®), doxorubicin, and prednisone (CHOP) versus cyclophosphamide, doxorubicin, vincristine (Vincasar®), and prednisone (CHOP) for the treatment of CD30-positive peripheral T cell lymphoma. 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.

Glutamine Independence is a Selectable Feature of Pluripotent Stem Cells.

Most rapidly proliferating mammalian cells rely on the oxidation of exogenous glutamine to support cell proliferation. The researchers in this study showed that reduced dependence on exogenous glutamine is a generalizable feature of pluripotent stem cells. The data reveal that reduced dependence on glutamine anaplerosis is an inherent feature of self-renewing pluripotent stem cells and that a simple, noninvasive mechanism to select for mouse and human pluripotent stem cells within a heterogeneous population during ESC passage induced pluripotent cell reprogramming.

Selected Clinical Trials

A Phase I Study of Brentuximab Vedotin Administered Sequentially and Concurrently with Multiagent Chemotherapy as Frontline Therapy in Patients with Systemic Anaplastic Large Cell Lymphoma
IRB: 11-092; PI: Steven Horwitz; Co-PI: Alison Moskowitz

This study was led by Steve Horwitz and published in The Lancet in January 2019. The study showed improved progression-free survival and overall survival for patients with newly diagnosed CD30 positive T cell lymphoma who received brentuximab vedotin (Adcetris®) with cyclophosphamide, doxorubicin, and prednisone (A+CHP) chemotherapy compared to patients who received standard CHOP chemotherapy: cyclophosphamide, doxorubicin, vincristine (Vincasar®), and prednisone (CHOP). This study led to the US Food and Drug Administration’s approval of brentuximab vedotin in combination with chemotherapy for the frontline setting for CD30 positive T cell lymphoma.

Phase II Study of Ruxolitinib in Relapsed or Refractory T Cell Lymphoma
IRB: 16-1542; PI: Alison Moskowitz; Co-PI: Steven Horwitz

This study demonstrated the efficacy of targeting the JAK/STAT pathway in patients with T cell lymphoma and showed preferential activity in T cell lymphoma characterized by JAK/STAT pathway alteration as well as in rare diseases, such as T cell prolymphocytic leukemia and T cell large granular lymphocyte leukemia. The data were presented at the 2019 annual meeting of the American Society of Hematology.

ME-401 for Relapsed/Refractory Follicular Lymphoma
IRB: 16-1614 and 19-246; PI: Andrew Zelenetz; Co-PIs: Anthony Mato (16-1614) and Connie Lee Batlevi (19-246)

ME-401 is an oral PI3k inhibitor that was evaluated in a phase I study led by Andrew Zelenetz for patients with relapsed/refractory indolent B cell lymphoma. While the development of PI3K inhibitors has been impeded by toxicity, this study showed that an intermittent dosing schedule of ME-401 (compared to continuous dosing) was associated with not only high efficacy but also reduced toxicity. This study with ME-401 has been integral to the development of PI3K inhibitors in follicular lymphoma. The efficacy and safety profile of intermittent dosing of ME-401 is now being further evaluated in a single-arm, multicenter phase II study of ME-401 in patients with relapsed/refractory follicular lymphoma.
Appointments, Promotions and Awards

Appointments

Sydney Lu
In October 2019, Sydney Lu joined the Myeloma Service as Assistant Attending Physician. He received an MD from Stanford University School of Medicine and a PhD from the Weill Cornell Graduate School of Medical Sciences, and he completed a residency in internal medicine at the New York Presbyterian Hospital/Weill Cornell Medical Center campus. Dr. Lu also completed a hematology and medical oncology fellowship at Memorial Sloan Kettering. Along with his work in the Myeloma Service, Dr. Lu is continuing to develop his translational research program in the laboratory of Omar Abdel-Wahab.

Urvi Shah
In April 2019, Urvi Shah joined the Myeloma Service as Assistant Attending Physician. She received an MD from the Grant Medical College and completed a residency in internal medicine at the Tufts Medical Center. Dr. Shah completed a fellowship in hematology and medical oncology at Montefiore Medical Center, the University Hospital for Albert Einstein College of Medicine. In July 2018, she joined the competitive Advanced Fellowship program Adult Cancer Immunotherapy at Memorial Sloan Kettering. Dr. Shah cares for Myeloma Service patients and participates in clinical research at MSK Commack and the David H. Koch Center for Cancer Care at MSK.

Eric Smith
Eric Smith was promoted to Assistant Member at MSK; Assistant Attending Physician in the Myeloma Service in MSK’s Department of Medicine; and Assistant Professor of Medicine at Weill Cornell Medical College.

Promotions

Awards

Sydney Lu
received a Robert Hirschhorn Endowment Award from the Portlock Challenge. These awards go to research fellows to fund their projects. Dr. Lu received $20,000 for his research. He presented his project, titled “Enhancing the Anti-Tumor Immune Response through Therapeutic Modulation of RNA Splicing,” at the Department of Medicine’s grand rounds on September 20th.

Urvi Shah
received a Future Leader in Hematology Award from Celgene in recognition of her clinical and translational research into plasma cell disorders.

Eric Smith
received a K08 award from the NCI for his project “Understanding and addressing sub-optimal responses to CAR T cell therapy for Multiple Myeloma.”

Francesco Maura
was named a recipient of the 2020 American Society of Hematology (ASH) Clinical Fellow Scholar Award.
Selected Publications

Role of AID in the Temporal Pattern of Acquisition of Driver Mutations in Multiple Myeloma.
Maura F, Rustad EH, Yellapantula V, et al. Leukemia. 2019;10.1038/s41375-019-0689-0. doi:10.1038/s41375-019-0689-0. PMID: 31836853

The role of activation-induced cytidine deaminase (AID) and the germinal center in multiple myeloma (MM) initiation has long been recognized. The chronological order of acquisition of single nucleotide variants in driver genes in 788 patients with MM was reconstructed in this study. A striking pattern emerged, reflecting the differential temporal activity of AID and Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like (APOBEC) during MM pathogenesis. More than 60 percent of MM patients have multiple large clonal chromosomal duplications, often acquired during the early phases of cancer development.

Genomic Landscape and Chronological Reconstruction of Driver Events in Multiple Myeloma.

The multiple myeloma (MM) genome is heterogeneous and evolves through preclinical and postdiagnosis phases. Sequences from 67 MM genomes serially collected from 30 patients, together with public exome data sets, were used to report a catalog and hierarchy of driver lesions. Focusing on whole genome sequencing data, complex structural events emerge as major drivers, including chromothripsis and a novel replication-based mechanism of templated insertions, which typically occur early. Hyperdiploidy also occurs early, with individual trisomies often acquired in different chronological windows during evolution, and with a preferred order of acquisition. Conversely, positively selected point mutations, whole genome duplication and chromoplexy events occur in later disease phases. Thus, initiating driver events evolve from a limited repertoire of structural and numerical chromosomal changes, shape preferred trajectories of evolution that are biologically relevant but heterogeneous across patients.

Association of Immune Marker Changes with Progression of Monoclonal Gammopathy of Undetermined Significance to Multiple Myeloma.

Multiple myeloma (MM) is consistently preceded by monoclonal gammopathy of undetermined significance (MGUS), and risk models that estimate the risk of progression from MGUS to MM use data from a single time point (usually the initial workup). This prospective cross-sectional cohort study included 77,469 adults age 55 to 74 years in the screening arm of the National Cancer Institute Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial who had a diagnosis of progressing MGUS (n=187) or stable MGUS (n=498), including light-chain subtype, from November 1993 through December 2011. Serum protein and monoclonal immunoglobulin levels, serum-free light chains, and serum light chains within each immunoglobulin class were measured. The findings of evolving risk patterns support annual blood testing and risk assessment for patients with MGUS or light-chain MGUS.

Minimal Residual Disease Negativity in Multiple Myeloma is Associated with Intestinal Microbiota Composition.

Patients with multiple myeloma (MM) who achieve minimal residual disease (MRD) negativity after upfront treatment have superior outcomes compared with those who remain MRD positive. The association between intestinal microbiota composition and treatment outcome in MM is described in this report. The microbiota composition of fecal samples collected from 34 MM patients after induction therapy and at the time of flow cytometry-based bone marrow MRD testing was determined by 16S ribosomal RNA sequencing. The potential association of microbiota composition with treatment response in MM patients is an important parameter for additional correlative and clinical investigation.

GPRC5D is a Target for the Immunotherapy of Multiple Myeloma with Rationally Designed CAR T Cells.

Early clinical results of chimeric antigen receptor (CAR) T cell therapy targeting B cell maturation antigen (BCMA) for multiple myeloma (MM) appear promising, but relapses associated with residual low to negative BCMA-expressing MM cells have been reported, necessitating identification of additional targets. Quantitative immunofluorescence was used to determine that the GPRC5D protein is expressed on CD138-positive MM cells from primary marrow samples with a distribution that was similar to, but independent of, BCMA. GPRC5D(109) CAR T cell therapy shows potential for the treatment of advanced MM irrespective of previous BCMA-targeted therapy.
INTERVIEW

Mashiyate Meem
Clinical Research Coordinator
Myeloma Service

What do you find most rewarding about your role?
The power of data transcends far beyond just numbers. When hearing the word “data,” people often think you are just entering numbers into a database, but it’s more than that. It tells the story and the journey of the patients, from when they were first diagnosed with cancer to the different drug therapies they received. Numbers also tell you how these drugs affected patients’ overall well-being and any reactions they had to them. It almost feels like being a detective putting all the pieces together.

How did you become interested in clinical research?
I have a keenness in problem-solving, and I loved working with numbers in general. I’ve also always been interested in oncology, so it excited me to be able to combine both of my passions at MSK.

How will your experiences in this role help you with your future goals and career development?
My main aspiration in the short term is to streamline processes in the databases and work on tackling larger projects conducive to cancer drug therapy. For the long term, I want to work on growing as a healthcare leader to ensure efficiency and progress in cancer treatment.

Who do you most look up to at work? Is there anyone you admire and, if so, why?
I particularly admire Chief of the Myeloma Service Ola Landgren. He is constantly maintaining amicable relationships with everyone on the team. He gets to know each of us on a personal level, which you don’t find with everyone. He always greets us with a friendly smile, and there’s always a twinkle in his eye, while leading some of the largest clinical trials and treatment strategies in the world.

What do you enjoy most about working at MSK?
I love that every single day that I come to work is a day spent helping save someone’s life. Every moment spent at work is for the greater good of the patients. That’s something you can’t say about just anywhere.
Bodies in Motion: How Biomonitoring Can Measure Outcomes from Multiple Myeloma Treatment

The blood cancer multiple myeloma tends to affect older adults. Many new therapies have been approved recently or are being developed for multiple myeloma. To choose the best treatment option for each patient, it’s important to understand how these different treatments affect older people and impact their quality of life.

Memorial Sloan Kettering hematologic oncologist Neha Korde is leading research to address this topic. At the American Society of Hematology’s annual meeting in December 2019, she presented early findings from a study aimed at assessing the health and wellness of people undergoing initial chemotherapy after being diagnosed with multiple myeloma.

“We know that when patients are first diagnosed, they are often having a lot of pain due to bone lesions,” Dr. Korde says. “We were really interested in looking at their mobility, because that’s a good way to measure how they are feeling. So we proposed doing a biomonitoring study.”

**Continuous Monitoring, Compelling Findings**

In the study, 40 people who had been newly diagnosed with multiple myeloma were given wearable devices to monitor their sleep and activity levels for about six months. (Garmin Vivofit devices were used.) Half of the participants were under age 65 and half were over age 65. The participants also regularly filled out questionnaires to report how they were feeling, including their levels of pain.

The patients were monitored 24 hours a day, seven days a week, starting with a baseline and throughout six cycles of chemotherapy. Data about their activity and sleep were automatically uploaded and paired with results from the surveys they filled out. “This gave us the opportunity to look at the objective data,” Dr. Korde explains.

Dr. Korde and her colleagues, including investigators in the Behavioral Research Methods Core, are continuing to analyze the data from the study, but they have already been able to identify trends. For example, they found that the baseline activity levels for younger people were much higher than for older people. Younger people averaged about 6,000 steps per day. During and after treatment, they showed only slight increases — of about 6 percent. In contrast, older people had much lower activity levels before treatment, just over 2,200 steps per day on average. But they showed a much higher increase during and after treatment — nearly 35 percent.

“There’s been a lot of worry about how well older people are able to tolerate treatment,” Dr. Korde explains. “These findings suggest that those over age 65 are much more impacted by the burden of their symptoms at the time of diagnosis than younger people are. They are much more immobile. Therefore, these older patients stand to benefit greatly in terms of mobility.”

**A Potential Monitoring Tool**

The investigators hope that activity monitoring will become a standard measuring tool that can be incorporated into clinical practice and, potentially, into future clinical trials.

“There are many new drugs coming out, and they’re being tested in different settings — for relapsed and refractory disease, as well as in those who are newly diagnosed,” she explains. “It’s important for us to figure out not only which drugs or drug combinations are most effective at treating the disease but also how they impact the patient’s quality of life.”

She adds that the biggest take-home message is that people who are elderly and fragile have the most to gain from treatment. “Balance is very important in this group of patients,” she notes. “If I select a treatment that makes someone feel very sick and puts them in the hospital, I’m not doing them justice.”

Dr. Korde says that another hope is that this tool can ultimately help influence interventions, rather than just be used as an observational tool. For example, it could help guide the use of drugs to treat side effects from treatment, including steroids.

Dr. Korde notes the benefits of doing this kind of research at a place like MSK. “This study took a lot of planning before we even launched it,” she says. “The biggest asset was being able to conduct the study in a hospital setting that specializes in cancer.” She also credits Information Systems Support within the Research and Technology Management division with helping her team collect and analyze the data.

**“The better we can understand what patients are going through during treatment from a functional standpoint, the more we will be able to help them maximize the benefit from these therapies.”**

Neha Korde
hematologic oncologist

“We’re lucky because therapies for multiple myeloma are getting better and better,” she concludes. “The better we can understand what patients are going through during treatment from a functional standpoint, the more we will be able to help them maximize the benefit from these therapies.”
**New York Magazine’s “Best Doctors” List**

**Ellin Berman** is an attending physician in the Leukemia service with a clinical and research focus on new drug development in acute and chronic leukemias, including acute myeloid leukemia (AML) and chronic myelogenous myeloid (CML). She is also listed as an Exceptional Women in Medicine in 2019 by Castle Connolly Medical Ltd and *New York Magazine.*

**Sergio Giralt** is the Deputy Division Head of the Division of Hematologic Malignancies and the Melvin Berlin Family Chair in Multiple Myeloma. He focuses his clinical practice and research on stem cell transplantation for patients with blood disorders. He has made significant contributions to the field of BMT, such as developing the use of reduced-intensity conditioning regimens for older or debilitated patients with blood cancer.

**Gerald Soff,** Chief of the Hematology Service, has extensive experience in the diagnosis and management of thrombotic diseases as well as hemorrhagic disorders. His research involves studies of the interaction of the coagulation system and cancer. He is also actively involved in training medical students, residents, and fellows in hematology.

**Martin Tallman,** Chief of the Leukemia Service and Cassidy Family Endowed Faculty Chair, focuses on the clinical investigation in acute myeloid leukemia, acute lymphocytic leukemia, acute promyelocytic leukemia, and hairy cell leukemia. Dr. Tallman is currently president elect of the American Society of Hematology (ASH).

**Andrew Zelenetz,** Medical Director of Quality Informatics, is an attending physician in the Lymphoma service. He has helped develop several agents now approved to treat lymphoma — including 131I-tositumomab/tositumomab, bortezomib, and pralatrexate — and through clinical studies he is evaluating the benefits of novel combinations of agents. In another area of research, he is working to improve the prognostic value of patients’ pathology specimens using computer-aided image analysis.
After years of planning and anticipation, the David H. Koch Center for Cancer Care at Memorial Sloan Kettering opened to patients in January 2020.

Located off York Avenue on 74th Street, the 750,000-square-foot center is staffed by about 1,300 people on 25 floors, with 230 exam rooms, 110 infusion rooms, 37 procedure rooms, and 16 inpatient beds for patients who may require a short stay. Because numerous specialties are available in this single location, patients can receive many of the services they need in one visit, reducing travel time and stress while also fostering face-to-face collaboration among care teams and specialists.

A primary goal is to ensure that everyone who enters the facility feels engaged, embraced, and empowered — MSK staff as well as patients. In October 2019, approximately 375 faculty and staff members moved into offices in the new building, and for the first time, the entire Division of Hematologic Malignancies was joined together under one roof. According to Paul Hamlin, Medical Director of the new center, “The opening of this facility represents a major step forward for our institution.”

The David H. Koch Center for Cancer Care at Memorial Sloan Kettering builds on MSK’s efforts to deliver the best possible patient experience, with an assist from easy-to-use technology. When patients check in, they are given a CarePass. This small electronic badge gives people the freedom to move around the entire building because staff can find them when they are needed — even down to a specific chair. This replaces waiting with exploring. Patients and their loved ones can discover spaces carefully designed to relax and recharge, as well as cafés, a shop, an outdoor terrace, and an extensive art collection, including a digital fish pond.

This intense focus on the patient experience extends to the Steven A. Greenberg Center for Clinical Trials, a floor devoted to early-phase clinical trials. The area was specifically conceived for the comfort and convenience of people taking part in studies of new therapies. “Patients in these trials may have to be here for an extended period of time,” says Elizabeth Rodriguez, Director of Nursing at the new facility. “An infusion may last as little as an hour, but follow-up tests, such as blood draws and EKGs, could keep patients in the building for longer.”

Integrating the experience, wisdom, and creativity of MSK’s staff into the design gave employees significant influence over the center’s approach to patient care and the patient experience. Employees’ impact can be seen throughout the building. The 58-chair infusion unit on the 15th floor features “mobility zones,” instead of a waiting room, giving patients greater choice in how and where to spend their time. This was a suggestion from Nursing, as were many of the innovative elements incorporated into the inpatient area.

Beginning in 1990, David H. Koch served as a member of MSK’s Boards of Overseers and Managers, and he made historic gifts and pledges to the institution. Though Mr. Koch died in August 2019, his profound commitment to MSK will live on through the center named in his honor and made possible through a $150 million donation — the largest single donation in MSK’s more than 130-year history.

The David H. Koch Center for Cancer Care at Memorial Sloan Kettering will allow MSK to expand access to the rapidly increasing number of people requiring outpatient care.
The ribbon-cutting ceremony for the David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center was December 10, 2019.
In January 2020, the David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center opened its doors to patients. For those receiving treatment for blood cancer at MSK in Manhattan, the new facility brings all the outpatient care within the Division of Hematologic Malignancies under one roof for the first time. It also houses several other clinical services within MSK.

The David H. Koch Center for Cancer Care at Memorial Sloan Kettering aims to create a new kind of clinical environment for patients and their caregivers, as well as for staff. It uses a number of cutting-edge technologies designed to improve the care of people with cancer while at the same time advancing research and innovation.

“When faced with a cancer diagnosis, patients lose a sense of control over their lives,” says medical oncologist Paul Hamlin, Medical Director of the David H. Koch Center for Cancer Care. “One of the goals in the design of this center was to give people back some of that control.” For example, people can move around the facility rather than sitting in a waiting room. Additionally, schedules and wait times are continually updated and communicated to patients in an effective way.

**Using Technology to Improve the Patient Experience**

A variety of spaces provide different environments for patients, whether they want to look at art, play games, do puzzles, or catch up with the office. They can also participate in yoga and meditation classes, work on craft projects, or visit with the Caring Canines, MSK’s therapy dogs. Through a system called MSK Carepass, staff can find patients when it’s time for their appointments.

In clinical examination and treatment rooms, technology to improve the patient experience really comes to the fore. “We’ve created a setting where it’s easier to share information,” Dr. Hamlin explains. Family members who can’t be physically present participate in consultations via a video portal. Off-site doctors can consult with patients face-to-face as well.

“This system allows us to seamlessly share clinical images, like lab reports or PET scans and CT scans, with the patient,” Dr. Hamlin says. “We can pull up video information about a clinical trial or about management of side effects, enabling us to improve people’s understanding of the care that they’re getting.”

In the infusion suites, where people receive chemotherapy and other treatments, a number of chairside resources are available. They can order food or access a variety of entertainment sources. They can also control the environment by making adjustments to the lighting and window blinds.

People receiving bone marrow transplants (BMTs) — whether allogeneic or autologous — receive consultations and at least some of
their treatments at the David H. Koch Center for Cancer Care at MSK. Cellular therapies, such as chimeric antigen receptor T cell therapy, are offered here as well. “Patients who have outpatient transplants can get all of their care here,” Dr. Hamlin says. The new center is located only a block from the MSK 75th Street Patient Residence, where those who are having outpatient transplants often stay during the first part of their recovery.

BMT patients who receive their transplants as inpatients still meet with their MSK doctors at the David H. Koch Center for Cancer Care during the times they are not hospitalized.

**Moving Clinical Science Forward**

Innovations throughout the new building also aim to advance clinical research. “Scientific advances and the understanding of blood cancer biology often benefit from more than one disease type — myeloma, lymphoma, and leukemia,” Dr. Hamlin notes. “Bringing everyone under one roof really does allow for that collaborative experience between clinicians and scientists.”

Another advance is that an entire floor is dedicated to early drug development. “First-in-human studies across the entire MSK community are being performed on the same floor,” Dr. Hamlin says. “There are nurses who are skilled in clinical trial procedures and a laboratory that is geared around the efficient care of patients receiving drugs for the first time — all in the same spaces.”

Teams at the David H. Koch Center for Cancer Care at Memorial Sloan Kettering are built on what Dr. Hamlin calls “a triad of leadership,” which consists of a physician, a nurse, and an administrator. “This collaboration across disciplines is woven into the very fabric of everything that we’re doing here,” he says. “We really hope that this collaboration will create a different feel to the environment.”

Having members throughout the Division of Hematologic Malignancies working in the same physical space also allows for more chance encounters, enabling ideas and collaborations to form organically, Dr. Hamlin concludes. “It’s much easier for everyone to attend grand rounds,” he says. “We created spaces on every academic floor that make it easier for people to come together.”
12th floor waiting room
Everyone who’s ever met Memorial Sloan Kettering employee Nick Medley has left their interaction with him feeling more positive and optimistic. Mr. Medley, Lead Guest Services Representative, has been making MSK patients, family members, and staff smile for almost 20 years — even in their most difficult moments.

“We try to help alleviate what patients and their families are going through,” he says.

Mr. Medley started working as a door attendant at the Rockefeller Outpatient Pavilion in 2001, after being laid off from an administrative position at an investment banking firm on Wall Street. He learned about the position through a former colleague. After six years in that role, he became a guest services representative at the Rockefeller Outpatient Pavilion.

In January 2020, he transitioned to the new David H. Koch Center for Cancer Care at Memorial Sloan Kettering Cancer Center. This is where patients treated by the Division of Hematologic Malignancies receive much of their treatment. He now moves back and forth between the two locations.

As a guest services representative, Mr. Medley helps connect patients to the resources that they need. This ranges from helping them get in touch with departments such as social work and counseling, to helping arrange transportation and ensuring that patients get home safely after their appointments. He also acts as a concierge of sorts, providing information about shops and restaurants that are nearby.

But more important than the duties that fall under his official job description, Mr. Medley provides emotional support for everyone who comes through the door. “When you’re coming in as a patient or a family member, your mind is racing,” he says. “You may be coming in for the first time after a cancer diagnosis, or you may be coming for treatment or test results. I can see the fear on their faces, and that’s when I step in — not only to assist them but to provide compassion and hope.”

He says that from the time he was young, his mother and grandmother called him an old soul. “I was always drawn to want to help people. Some people call it a gift, and it’s always been part of my spirit,” he says. “It’s no accident that I ended up here. I feel that I was called to do what I’m doing, and I feel grateful for that.”

Mr. Medley praises the facilities at the David H. Koch Center for Cancer Care at Memorial Sloan Kettering, which was designed to give people a feeling of safety and serenity. “The building provides an atmosphere of peace. It doesn’t feel like a hospital,” he says. “It’s really beautiful, and it helps put people in a different frame of mind.”
Opening of MSK Nassau

In April 2019, Memorial Sloan Kettering opened MSK Nassau, expanding its cancer care in Nassau County on Long Island. The new facility, in Uniondale, includes a number of features designed to make treatment easier and more convenient. MSK’s location at Rockville Centre, which opened in 1997 on the campus of Mercy Medical Center, has closed. All patient care, staff, and services from Rockville Centre relocated to the new site. MSK Nassau’s opening allows for more-convenient treatment for people from Nassau County and eastern Queens.

Encompassing 114,000 square feet and including more than 300 dedicated medical and professional staff, MSK Nassau offers almost every aspect of outpatient cancer care: infusion services (chemotherapy and blood transfusions), medical oncology, radiation therapy, radiology and imaging services, screening services (including mammography), personalized medicine, genetic testing, support counseling, and follow-up care. The facility also features a full-size rehabilitation suite — a first for MSK on Long Island — that includes a gym with the latest equipment as well as a private room for lymphedema treatment.

Patients benefit from the most-innovative technologies available to help diagnose, monitor, and treat cancer, including highly sensitive imaging tests, such as PET, CT, MRI, and ultrasound; precise tools used to deliver radiation therapy; the most-advanced pathology testing, including the latest molecular diagnostics for personalized medicine; and immunotherapy. Patients also have access to MSK’s robust clinical trials program, including early-stage studies of novel targeted anticancer drugs.

Great care was taken to ensure that MSK Nassau offers a warm, welcoming environment. The infusion suite includes chair-side technology, allowing patients to control the lighting and temperature in their area and providing access to cable TV, Internet, and educational videos produced by MSK experts from such departments as Integrative Medicine, Nutrition, Nursing, and others.

The first- and second-floor waiting areas feature floor-to-ceiling windows for natural light, game tables, and private seating. The facility also displays numerous pieces of art, some of which show Long Island landscapes and cover entire walls, and a community art gallery with artwork on loan from local artists.
Faculty from the Division of Hematologic Malignancies
Currently Practicing in the Regional Network

**MSK Basking Ridge**
- Audrey Hamilton
  Lymphoma Service
- Anita Kumar
  Lymphoma Service
- Anthony Mato
  Leukemia Service

**MSK Monmouth**
- Virginia Klimek
  Leukemia Service
- Neha Korde
  Myeloma Service
- Colette Owens
  Lymphoma Service

**MSK Bergen**
- Neha Korde
  Myeloma Service
- Matthew Matasar
  Lymphoma Service
- Michael Mauro
  Leukemia Service

**MSK Nassau**
- Lorenzo Falchi
  Lymphoma Service
- Erel Joffe
  Lymphoma Service
- Oscar Lahoud
  ABMT service

**MSK Commack**
- Oscar Lahoud
  ABMT service
- Ildefonso Rodriguez-Rivera
  Lymphoma Service
- Urvi Shah
  Myeloma Service

**MSK Westchester**
- Philip Caron
  Lymphoma Service
- Hani Hassoun
  Myeloma Service
- Andrew Zelenetz
  Lymphoma Service
**Targeted Drug Could Improve Treatment of T Cell Lymphomas**

T cell lymphoma is a rare type of non-Hodgkin lymphoma that too often recurs after initial chemotherapy. Better therapies are urgently needed for many patients, and MSK researchers have been testing targeted therapies that turn off the molecular pathways that drive T cell lymphoma to grow.

Two pathways that move through molecules called SYK and JAK seem to play an important role in promoting two forms of T cell lymphoma to grow: peripheral T cell lymphoma (PTCL) and cutaneous T cell lymphoma (CTCL). A study of genetic mutations found in these cancers suggests that the cells may grow faster and survive because of multiple molecular signals within these pathways.

A targeted therapy called cerdulatinib, which is taken as a pill, has shown potential in other blood cancers because it inhibits both the SYK and JAK pathways. At the ASH meeting, MSK medical oncologist Steven Horwitz presented findings from a phase II study testing cerdulatinib in 61 people with PTCL or CTCL that didn’t go away or came back after other treatments. The drug appears to be safe and somewhat effective in both lymphoma types, primarily in specific subtypes.

Cerdulatinib seems to work especially well against a specific type of PTCL called angioimmunoblastic T cell lymphoma. In this group of 22 people, 41 percent had a complete response, meaning no tumors were detectable by PET scan after treatment.

Dr. Horwitz says this means that in addition to finding a new treatment to help people with T cell lymphoma, researchers may be able to identify a molecular marker that better predicts whether the treatment will work in a specific person.

“If you can understand what determines whether a drug works, it makes it possible to more intelligently design combination therapies, which is where we think these targeted therapies will be able to make the greatest impact against lymphomas,” he says.

**Combination Therapy Shows Promise in Hodgkin Lymphoma**

Hodgkin lymphoma is usually curable with chemotherapy and radiation, but some people don’t respond to treatment or the disease comes back. Until recently, the second-line treatment for these patients typically involved combinations of fairly toxic chemotherapy aimed at wiping out the cancerous cells.

In the last decade, two new drugs have been approved for patients with recurrent Hodgkin lymphoma. Brentuximab vedotin (Adcetris®), approved in 2011, is an antibody linked to a cancer-killing toxin. Nivolumab (Opdivo®), approved in 2016, is an immunotherapy drug that blocks the actions of a molecule called PD-1 on the surface of immune cells.

Researchers have been investigating whether combining brentuximab vedotin and nivolumab can be even more effective. Last year, encouraging results were reported from a phase I/II clinical trial testing the drug combination in people with relapsed or refractory Hodgkin lymphoma.

Dr. Moskowitz says. In addition, the two-year progression-free survival rate was 79 percent. Progression-free survival is the time the cancer remains under control without getting worse.

“This indicates that we have a high chance of curing patients in the second-line setting with a well-tolerated treatment,” she says.

“This field is evolving really quickly.”

**Using Nanoparticles to Treat Diffuse Large B Cell Lymphoma**

Diffuse large B cell lymphoma (DLBCL), an aggressive cancer of white blood cells, seems to offer an especially inviting target for drugs. A protein called BCL2 appears to play a key role in helping lymphoma cells survive, and a BCL2 inhibitor called venetoclax (Venclexta®) has been effective in people with another blood disease called chronic lymphocytic leukemia.

However, venetoclax has not worked as well as expected in people with DLBCL. The problem is that in DLBCL cells, BCL2 appears to have a backup actor—a protein called MCL1. Blocking BCL2 only is not enough to kill most DLBCL tumors because the cancer cells can still rely on MCL1 to survive.

In 2018, a team led by medical oncologist Anas Younes showed that blocking the BCL2 and MCL1 proteins with a two-drug combination effectively killed DLBCL cells in a lab dish and in mouse models. However, this combination therapy also appeared to be toxic when used at sufficient doses to stop the cancer.

At the 2019 ASH meeting, Neeta Bala Tannan, a postdoctoral researcher in the Younes laboratory, presented details on a potential way to reduce this toxicity using tiny particles called nanoparticles. These nanoparticles are designed to home in on an inflammatory protein called P-selectin, which is found in abundance in blood vessels that nourish cancer cells. When loaded with either venetoclax or an MCL1 inhibitor called S63845, the nanoparticles can ferry the drugs selectively to the DLBCL cells.

In mouse models, this precise delivery enabled researchers to lower the drug dosage because it was getting to the right spot. Using the nanoparticles to deliver either drug—even if the other was given without nanoparticles—lowered toxicity while effectively treating the cancer.

“This novel drug delivery approach shows promise for improving treatment of DLBCL by increasing effectiveness while reducing treatment-related toxicity, but it still needs to be tested in people,” Dr. Younes says.
Multiple myeloma is a cancer that arises from the type of white blood cells called plasma cells. When normal plasma cells in the bone marrow develop certain genetic mutations, they may turn into myeloma cells.

At the 2019 annual meeting of the American Society of Hematology (ASH), Memorial Sloan Kettering researchers reported on some of the latest advances in detecting and treating multiple myeloma.

A New Combination Therapy

One of those studies, led by MSK hematologic oncologist Ola Landgren, Chair of the Myeloma Service, is a phase II clinical trial looking at a new combination of drugs for those recently diagnosed with multiple myeloma.

In this trial, the participants had a targeted antibody drug called daratumumab (Darzalex®) added to a standard chemotherapy combination, called KRD, which is comprised of three drugs: carfilzomib (Kyprolis®), lenalidomide (Revlimid®), and dexamethasone (Ozurdex®).

“After someone completes treatment for multiple myeloma, the measure of how effective that treatment was is called minimal residual disease, or MRD,” Dr. Landgren explains. “MSK uses two very sensitive tests that can detect a single cancer cell in 100,000 or more plasma cells. If we can’t find any cancer, we feel quite confident the treatment has been successful.”

Among the 30 people who got the KRD-daratumumab combination, 77 percent of them were MRD negative after eight cycles of treatment. Based on cross-study comparison, the average level of MRD negativity seen with other therapies is 54 percent for those who get KRD alone, 58 percent for those who get KRD followed by an autologous stem cell transplant, and 59 percent for those who get a different chemotherapy combination called VRD-daratumumab followed by a transplant.

Daratumumab is currently approved by the US Food and Drug Administration for use in people who are unable to have transplants because of age or other health problems. Dr. Landgren says that based on these findings and other emerging studies, he thinks daratumumab could be used more widely.

Along with the biotech company Amgen, Dr. Landgren is working with the FDA to develop a large, randomized, multicenter clinical trial designed to evaluate KRD-daratumumab in comparison to the drug combinations that are currently considered the standard of care. He says that if the new combination is shown to be effective in a head-to-head comparison with current standard treatments, it could lead to wider approval of the drug.

“It’s too early to say that the addition of daratumumab to KRD, as a consequence of the high rate of MRD negativity, will result in an increasing proportion of newly diagnosed multiple myeloma patients opting for delaying their transplants, but it’s possible that may be the case,” he says. “Transplants are effective, but they are also associated with significant short-term as well as long-term toxicities, whereas side effects from daratumumab are quite minimal. The current phase II study is limited by small numbers and short follow-up, but the early results showing 77 percent of patients with no MRD are very exciting.”

Learning How Multiple Myeloma Develops

Another important study looked at the early development of multiple myeloma. The disease is diagnosed in about 32,000 people in the United States every year, but experts estimate that, by age 60, many more people — from 3 percent to 5 percent of the population — will have cells detectable in their blood that show signs of pre-myeloma.

These myeloma precursors can develop years or even decades before symptoms of the disease begin to develop. The symptoms include bone pain and frequent infections. Since the discovery of these early changes was made about ten years ago, the challenge has been determining who is most likely to develop the disease — and therefore should consider closer observation or possibly treatment — and those who don’t need to worry.

In the new research, an international group of investigators led by MSK hematologic oncologist Francesco Maura, a member of Dr. Landgren’s lab, developed a computational algorithm to understand when the first genetic driver of these pre-myeloma cells is acquired. Using genetic information from samples collected through two large, public databases, the researchers were able to reconstruct the life history of these blood cells long before the myeloma developed.

“We were quite surprised to find that many of the key changes associated with myeloma are acquired when people are in their 20s and 30s, even though the average age of disease onset is 63,” Dr. Maura says. “In this study, we developed a way to find the tumor cells’ mutation rate by looking at when the key drivers are accumulated and the degree to which they contribute to the formation of cancer.”

One of the main goals of this research is to understand who has a high risk of ultimately developing cancer so that it can be treated before symptoms start. “We also know that as it progresses, multiple myeloma develops additional mutations that make it more aggressive and harder to treat,” Dr. Maura says. “Ideally, we would want to eradicate the cancer when it is less complex.”
The annual meeting of the American Society of Hematology (ASH) brings together leaders from around the world who treat people with blood cancers and other blood disorders. Doctors and researchers from Memorial Sloan Kettering presented their research at the meeting, held in December 2019 in Orlando. Below are some highlights.

**The Latest on CAR T, New Treatments for CLL, and Using Genes to Predict a Common Side Effect**

By Matthew Tontonoz

The scientists were curious to find out if a group of patients would benefit from the procedure. Of 53 adults with ALL who received CAR T cells at MSK, 16 of those who had a complete response to the CAR therapy went on to have a stem cell transplant. Dr. Park and his colleagues looked for correlations between how well these patients did and several variables: age, a prior stem cell transplant, the presence of the Philadelphia chromosome, the amount of disease measurable at the time of the CAR therapy, the severity of cytokine release syndrome, and neurotoxicity.

The only variables that seemed to make a difference were age and neurotoxicity. Specifically, being younger and having no severe neurotoxicity during CAR therapy were associated with improved overall survival following a stem cell transplant. Dr. Park cautioned that the small size of the study limits drawing firm conclusions. Nevertheless, the results point to a group of people for whom the potential benefits of a stem cell transplant may outweigh the risks. Further research is needed.

**Advances in CLL**

MSK hematologist-oncologist Anthony Mato presented the results of several studies aimed at improving care for people with chronic lymphocytic leukemia (CLL). One study dealt with identifying the best treatment options for people with CLL who have had to stop taking the targeted drug venetoclax (Venclexta®). Dr. Mato and colleagues conducted a retrospective study of 326 people with CLL from around the world who received venetoclax and then switched to another drug. They looked at how well these people did on various treatments — specifically BTK inhibitors, PI3K inhibitors, CAR T therapy, and stem cell transplantation. Of these, they found that BTK inhibitors were an effective post-venetoclax treatment, provided the patients had not yet received BTK inhibitors or had not developed resistance to these drugs. They also found that a stem cell transplant was a good option that provided lasting benefits.

In a second presentation, Dr. Mato discussed the results of a first-in-human trial of a BTK inhibitor called LOXO-305. This targeted drug works differently than existing BTK inhibitors. The trial, which enrolled 13 people, showed that LOXO-305 was safe. It also provided proof of concept that this targeted drug works differently than existing BTK inhibitors. The only variables that seemed to make a difference were age and neurotoxicity. Specifically, being younger and having no severe neurotoxicity during CAR therapy were associated with improved overall survival following a stem cell transplant. Dr. Park cautioned that the small size of the study limits drawing firm conclusions. Nevertheless, the results point to a group of people for whom the potential benefits of a stem cell transplant may outweigh the risks. Further research is needed.

**Car T and Stem Cell Transplants**

Chimeric antigen receptor (CAR) T cell therapies were in the spotlight at the ASH meeting. Many scientists in the field are excited by the prospect of using the genome-editing tool CRISPR to engineer more-potent CAR T cells.

At MSK, researchers Michel Sadelain, Renier Brentjens, and Isabelle Rivière and their colleagues are at the forefront of CAR T science. Just last year, the team published results from the longest-running clinical trial of CAR therapy, showing which patients benefitted most. At ASH in 2019, another member of that team, MSK medical oncologist Jae Park, presented the results of a retrospective study of 326 people with CLL who lacked an approved treatment option. Dr. Mato and his colleagues found that this combination, named DTRM-555, was generally safe and showed signs of effectiveness in several people. A phase II study of the combination is underway.

“Together, these studies show the progress we at MSK are making in developing much-needed therapies for people with CLL,” Dr. Mato says.

**Blood Clots and Cancer**

Blood clots are a life-threatening side effect in people being treated for cancer. Known risk factors for blood clots include cancer type and stage, obesity, blood cell counts, and treatment with chemotherapy. However, it is still difficult for doctors to predict the risk of blood clots in individual people. To find out if a tumor’s molecular profile could predict the risk of blood clots, MSK hematologist Simon Mantha and colleagues conducted a study in which they analyzed tumor DNA sequences for 341 genes in 11,695 people with cancer.

As Dr. Mantha presented at the ASH meeting, the scientists found that mutations in several genes — **STK11**, **MET**, **KEAP1**, **CTNNB1**, and **KRAS** — increase the risk of blood clots in people with cancer.

Dr. Mantha hopes these findings will ultimately translate into better methods to predict who is most at risk for this dangerous complication.

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**Photo: © ASH/Scott Morgan 2019**
2019 AMERICAN SOCIETY OF HEMATOLOGY (ASH) MEETING

Alumni Event at the 2019 American Society of Hematology Meeting in Orlando

More than 25,000 people attended the 2019 annual meeting of the American Society of Hematology (ASH) with great representation from our division. Research and advances to highlight include chimeric antigen receptor (CAR) T cell therapy and the microbiota, CAR T cells for multiple myeloma, targeting peripheral T cell lymphoma, acute myeloid leukemia, smoldering multiple myeloma and microbiota, and graft-versus-host disease after a bone marrow transplant.

The 12th annual ASH reception for the Division of Hematologic Malignancies was hosted by the Memorial Hospital Alumni Society at the Rosen Centre Hotel in Orlando. It was attended by MSK alumni, current faculty, fellows, and colleagues from other institutions as well as the division’s invited guests.
Christina’s Story: Why I Donated Stem Cells to Someone I’ve Never Met

By Christina Muggeo

In the summer of 2018, Memorial Sloan Kettering project manager Christina Muggeo received an unexpected phone call: She was a possible match for a cancer patient who needed a stem cell transplant.

Stem cell transplants, often called bone marrow transplants, are typically used to treat certain types of leukemia and lymphoma, as well as some other blood disorders.

In an allogeneic transplant procedure, blood stem cells from a donor are added into the bloodstream of someone with cancer, to replace the defective cells that have been knocked out with chemotherapy. Here, Ms. Muggeo describes her experiences as a stem cell donor and why she felt compelled to help a man she had never met.

I registered to be a blood stem cell donor when I was still in college, before I worked at MSK. They were having a drive on campus. I wasn’t sure exactly what it entailed, but the volunteers explained that I could be a potential match for a cancer patient. All they needed was a cheek swab.

When I found out years later that my cells were a match for someone with cancer, I immediately knew that I wanted to help. Through my work at MSK, as well as friends and family members, I’ve known many people with cancer. I know what they go through, and I had no hesitation about donating.

Seven Months before the Donation: A Waiting Game
It can take a few weeks to several months between getting the initial call and completing the donation procedure. I had some blood tests to confirm I was a match. I didn’t tell my family and friends right away because I wanted to be absolutely sure it was official.

When the match was confirmed, one of the first people I talked to was Marcel van den Brink [head of MSK’s Division of Hematologic Malignancies, who is an expert in bone marrow transplants]. I had worked in his office prior to my current role at MSK. I reached out to ask him what I should expect, both from the injections and from the procedure, and how I could alleviate any side effects. I also wanted to learn more about my match’s rare type of cancer.

While I was working with him, I helped organize fundraisers for DKMS, the nonprofit organization that had contacted me about my match. I was familiar with the work they do because Dr. van den Brink is on their medical board. He was very surprised that I’d been contacted about being a donor, because the odds of being matched to someone who is unrelated are quite low. It was an amazing coincidence, especially because the match was based on the sample that I’d given them back in college.

Two Months before the Donation: Learning about the Process
When I first got the call that I was a match, I was a little nervous. My friends and family were anxious as well. But it turned out that I was able to donate using a procedure called a peripheral blood stem cell donation.

This type of donation doesn’t require surgery. Instead, the stem cells are removed from the blood with a process called apheresis. Before the donation, you need to take a drug called filgrastim (Neupogen®) that boosts your body’s natural production of blood stem cells. The blood is taken out through a needle in your arm, the stem cells are removed from your blood, and the rest of the blood is put back through your other arm. This is similar to the process for donating platelets.

Five Days before the Donation: Flu-Like Symptoms
When the process began, I received injections of filgrastim for five days leading up to the donation. I was told I was likely to experience flu-like symptoms from the drug, but the side effects for me were very minor. The side effects I did experience were easily lessened with rest and relaxation at home.

The Day of the Donation
On the morning of the procedure, I ate a large breakfast to prepare for the day. I then headed to the New York Blood Center filled with excitement and a few nerves. I was there for several hours while they filtered the stem cells from my blood. I was truly surprised about how easy and nearly painless the process was.

Within 24 hours, I felt completely back to my normal self.

Why I Decided to Donate
While I don’t know much about the patient who received my stem cells, I’ve imagined everything he must be going through. He’s a total stranger, but I know the toll cancer can take on someone and wanted to help immediately. When I learned more about my match, I immediately thought of my father, because they’re around the same age. This quickly put things into perspective and calmed my fears. I hope that eventually I will get to meet him. In the meantime, DKMS has arranged for us to write letters to each other anonymously.

If I could talk to my match now, I would send him all my best wishes, ask him to stay strong, and let him know that he’s in my thoughts. I really hope that the transplant is successful and gives him another chance at life, because he still has so many years yet to experience.

Our mission at MSK is to treat and care for our cancer patients while finding a cure, so that’s exactly why I decided to donate. Cancer is a devastating disease and the impact that donors have should not be minimized. MSK employees are incredibly dedicated to our patients, so this opportunity was a unique way for me to give back.

For those who are unsure about registering to be a donor, I want you to know how easy it is to swab your cheek and send in the sample. It could be weeks or years before you get the call, or you may never be called. But just the possibility of being able to give someone with cancer hope is incredibly fulfilling. Wouldn’t you want to give someone who needs a transplant the chance to find a match?
Some People Who Need a Bone Marrow Transplant Will Never Find a Donor — and What Can Be Done about It

By Julie Grisham

For many people who have leukemia, lymphoma, or certain other blood disorders, stem cell or bone marrow transplantation (BMT) offers the best chance of a cure. But only about 25 percent of people who need an allogeneic transplant (the type of transplant in which donor cells are used) have a sibling who is a suitable genetic match. The remaining 75 percent usually look to registries of unrelated adult volunteers to find a compatible donor.

A study from investigators at Memorial Sloan Kettering reports that for people of certain racial and ethnic backgrounds, finding an unrelated donor match can be difficult if not impossible. This is despite huge growth in the pool of volunteer donors who have joined these donor registries — tens of millions in recent years.

“Our research demonstrates that many people will never find a matched volunteer donor from any registry because of their racial and ethnic background,” says lead author Juliet Barker, Director of the Cord Blood Transplantation Program. “For this increasingly large group of the US population, finding for research into alternative donor options, such as cord blood transplantation, is important.”

Cord blood is collected from the umbilical cord and placenta of healthy newborns and donated by the baby’s parents at birth.

Finding a Matched Donor

As the US population becomes more diverse, problems with finding matched donors will impact more and more transplant centers all over the country.

The study, published in Blood Advances, followed 1,312 people treated at MSK between 2005 and 2017 who needed a BMT but did not have a suitably matched sibling. The patients were categorized by their racial and ethnic backgrounds based on how they identified themselves and their family history. Thirty-four percent had non-European backgrounds. This included patients of Asian, white, Hispanic, African, Middle Eastern, and other mixed non-European descent.

“MSK is an ideal center to do this kind of study because our patient population is so diverse,” Dr. Barker says. “And this study is important as the US population is increasingly becoming more diverse: The problem of finding matched donors will impact more and more transplant centers all over the country.”

The researchers also reported that despite the notion that people of European descent can more easily find donors, many patients of southern European ancestry had diverse HLA markers and therefore were not able to find a match. This includes people from such places as southern Italy and Greece.

The Science of HLA Matching

Stem cell donors and bone marrow transplant recipients must be matched for their tissue type. Specifically, the matching process looks at markers, or proteins, known as human leukocyte antigens (HLAs). HLA markers are inherited and allow the immune system to recognize which cells belong and which are foreign. Over hundreds of generations, humans in different parts of the world have acquired many different HLA genes. Some people, such as those from Africa, have very diverse HLA types.

A close HLA match is critical when transplanting blood and bone marrow–forming stem cells from an adult donor to a patient. This makes it difficult for people of certain races or mixed ancestry to find a match.

By contrast, cord blood transplants do not require a strict HLA match. Another important finding from the study was that cord blood was able to extend transplant access to people from a wide variety of racial and ethnic backgrounds.

Benefits of Cord Blood Transplants

Cord blood is a rich source of blood-forming stem cells. Like stem cells from adult donors, cord blood is obtained through donor registries. Dr. Barker is an expert in this type of transplant and leads MSK’s Cord Blood Transplantation Program.

“A major advantage of cord blood is that the immune system of a newborn baby is not yet fully developed. This means that the match that’s required between the cord blood cells and the cells of the person receiving them is less strict,” Dr. Barker explains. “But in order to have a matched sibling, MSK doctors can very quickly determine, based on the patients’ HLA markers, whether they are likely to find a match in unrelated volunteer donor registries. She says this allows doctors to move very efficiently to alternative donor options for the transplant. “Timing is especially important,” she says. “Many patients will be too sick to have any kind of transplant if they wait too long.”
Nocturnists provide coverage for the entire medical service at Memorial Sloan Kettering from 7 PM to 7 AM. They handle 40 percent of admissions in the Department of Medicine. Kathleen Atlas, Head Nocturnist, and nocturnist Jamie Riches say that working at night, sacrificing sleep, and caring for critically ill patients is often grueling. But being in the presence of such strong individuals inspires them to make patients as comfortable as possible and to keep each interaction close to their hearts.

In November 2019, the Division of Hematologic Malignancies hosted the Second Annual Nocturnist Social. This event fosters relationships between nocturnists and doctors within the division.

The division sponsors Nocturnist Dinner Seminars as well. Nocturnists do not have access to many of the lectures and educational opportunities available during the day, due to their schedules. The seminars in the series are held in the evenings, so nocturnists are better able to attend. Several attendings in the division have presented including Gerald Soff, Chief of the Hematology Service; Miguel-Angel Perales, Deputy Chief of the Adult Bone Marrow Transplant Service; and Craig Sauter, Clinical Director of the Adult Bone Marrow Transplant Service.

Nocturnists and the Division

Kathleen Atlas, Head Nocturnist

Barbara Egan, Chief of the Hospital Medicine Service

Yvette Murillo, Night Advanced Practice Providers Group Lead

Nocturnists
Stacy Lee Anderson
Amare Assefa
Haaris Beg
Vicky Chiang
Ross Ehmke
Johann Hasbun
Bradley Lankowsky
Karen Ma
Elizabeth Maina
Liana Nisimova
Vijaya Venkatasubbarya Pavan
Kedar Mukthinuthalapati
Chika Ijeoma Okoli
Dhwani Patel
Ariel Peleg
Anna Yue Qiu
Jamie Riches
Joie Singh
Evan Stewart
Timothy Tiutan
Liubou Uslar
Joseph Wallins
On the Front Lines: Meet the Specialized Nurses Helping Move Cancer Research Forward

By Heather M. Graham

It was Monday, July 2, 2018, and the early morning air in Manhattan was humid, thick with anticipation for the upcoming Independence Day holiday. Memorial Sloan Kettering clinical trials nurse Kristen Clemens arrived at the Rockefeller Outpatient Pavilion and grabbed a free, if not delicious, cup of coffee from the vending machine before checking email and running through her list of patients for the day.

For eight years, Ms. Clemens worked as an inpatient nurse, caring for people in the hospital as they recovered from surgery and underwent cancer treatment. But in 2017, she joined the ranks of a specialized nursing team at MSK that’s responsible for caring for patients who enroll in first-in-human clinical trials. These studies are the first time a new drug is given to a human being, so the relationships between nurses and patients take on an added level of trust and partnership.

“First-in-human trials are done to establish a standard therapeutic dose of a new cancer drug and to make sure it’s safe and effective in people,” says Ms. Clemens. “That means that my patient could be one of a handful of humans — or maybe even the very first human — to receive what could become the next blockbuster cancer treatment. It is really special when someone volunteers to participate. For me as a nurse, it adds an entirely different dimension to the time we spend together, especially in the moments when they receive their very first dose.”

As she prepared to see her first patient that July day, Ms. Clemens confirmed, again, that everything was ready: the other nurses knew what to expect, the research assistants were looped in, the infusion was ready and waiting to be picked up from the pharmacy. This drug was known for causing an infusion reaction, so there was a plan for that, too.

Ms. Clemens entered the exam room to see her patient, a woman in her 50s. She had recently come to MSK with a stage IV lung cancer diagnosis to get a second opinion on her treatment options. She’d already undergone chemotherapy and radiation and, after careful consideration, had decided her best option was to participate in a clinical trial. She would become one of the first people, and the first MSK patient, to receive a new kind of treatment: a cancer vaccine made from the tissue of the lung tumor that was threatening her life. “Unlike preventive vaccines, such as the one you get to protect from the flu, this trial uses a therapeutic, or treatment, vaccine. It is an injection of a small amount of the thing that makes you sick. This triggers the immune system to recognize what cells to go after and kill,” Ms. Clemens says.

Three months prior, MSK interventional radiologist Yolanda Bryce had taken a needle biopsy of the woman’s lung tumor. Next, the MSK research team led by medical oncologist Matthew Hellmann prepared and sent the small tissue sample to a lab in Germany, to create a vaccine designed to attack and destroy the patient’s cancer.

When the time came for the infusion, Ms. Clemens turned to her patient. “Are you ready to do this thing?” she asked.
**First in Human**

“At some point, medicines that have shown great promise in the lab have to be given to humans,” says Eytan Stein, Director of the Program for Drug Development in Leukemia at MSK. “We are very lucky to have such a world-class team of doctors, nurses, and researchers, people with the expertise to take care of our patients who volunteer to be part of first-in-human clinical trials here at MSK, which has one of largest programs in the country.”

Every year thousands of patients participate in clinical trials at MSK. “Some patients are sent to us because they have exhausted the standard treatment options for their cancer,” says Dr. Stein. “But we encourage our patients to consider a clinical trial from the very start of treatment if there’s one that’s right for them. This allows patients the opportunity to receive the most-advanced cancer treatments available, sometimes years before they’re offered anywhere else.”

A first-in-human trial requires a substantial patient care team. Principal investigators, such as Dr. Stein, oversee the trials and evaluate patients, their medication dosages, and tests while continuously analyzing the trial’s results. Clinical trials nurses manage daily patient care and keep trial data accurate and up-to date.

They monitor patients to treat new symptoms early, and quickly, so patients can remain on a treatment longer if it’s effective. If side effects become too intense, or if the drug is not working, the dose is adjusted or the medication is stopped, especially if the cancer is getting worse.

“Without nurses, I wouldn’t be able to do my job,” Dr. Stein says. “Nurses assess and help manage toxicities and coordinate the tests that are crucial to understanding how these new drugs affect patients. They make sure that patients understand their treatment and receive the support they need to successfully participate in the clinical trial.”

**Patient Care**

Treating patients in clinical trials is Stephanie Hicklin’s specialty. “I wanted to be a clinical trials infusion nurse because we are at the forefront of cancer research while still providing direct patient care,” she says. To provide that care, Ms. Hicklin must quickly learn every trial protocol. This detailed guide of how to run a study includes how much of the drug to administer and the timing of follow-up tests, such as blood work.

“It can sometimes be scary for patients and their families because they don’t know how they’re going to react or if it is even going to work,” Ms. Hicklin says. “But I remind them that the whole team will be here every step of the way supporting them through it.”

Robert Rose, 67, sees Ms. Hicklin every Friday in the Developmental Treatment Unit on the fourth floor of the Rockefeller Outpatient Pavilion. He has kidney cancer and is participating in a unique first-in-human immunotherapy trial that combines nivolumab (Opdivo®), which is approved to treat advanced kidney cancer, with an investigational drug called IL-10, which he injects into his belly every day. During each visit, Ms. Hicklin takes his vital signs, draws blood, and performs any other lab tests requested, such as an EKG.

They also do a little catching up. “We talk about who’s expecting a baby, what’s going on with each other’s families,” says Robert.

Then it’s time for him to go upstairs for his checkup — where, thanks to the close collaboration among the clinical trials team, Ms. Clemens already has his results.

“Do you have any new symptoms?” Ms. Clemens asks while she examines Robert. She also inquires about his existing side effects. How’s the fatigue level? Still feeling unusually cold?

**Success and Setbacks**

Ms. Clemens notes that there can be disappointments in first-in-human trials. The first MSK patient on the personalized cancer vaccine trial was taken off the study after her lung cancer progressed and is exploring other treatment options with her doctor. But other patients on the same trial are stable, with no additional cancer growth, Ms. Clemens reports. Robert is thriving on his trial, too.

“He is back to gardening and growing tomatoes,” Ms. Clemens says. “His tumors shrank or disappeared, and he was able to see his daughter get married a few months ago.”

Still, successes with first-in-human clinical trials are few and far between, which makes it challenging to find the funding. “Philanthropy plays a crucial role in getting first-in-human trials off the ground, especially for rare diseases for which large pharmaceutical companies may not be focusing their efforts,” Dr. Stein says.

“There are never any guarantees that a treatment will work for everyone, but the hope that it might help someone really bonds me to my patients in a deeper way,” says Ms. Clemens. “Without these patients, discovering new medications wouldn’t be possible. They’re very brave.”

Ms. Hicklin is proud to be on the forefront of potential breakthroughs with her patients and fellow nurses. “Clinical trials are providing more treatment options for patients, helping people live longer, and ultimately bringing us closer to a cure. The work that we are doing is changing the future of cancer care,” Ms. Hicklin says. “And that is a really cool thing to be a part of.”
Nursing and APP Publications, Presentations, and Recognition

Honors
Meagan McQuade received the Samuel and May Rudin Award for Excellence in Nursing Practice.

Promotions
Julie Kleber, Hannah Morse, Brittney Pacheco, and Addi Watters were promoted to Clinical Nurse III.
Kelley Anderson, Anna Custodio, and Jenny Tran were promoted to Clinical Nurse IV.

Certifications
Daniela Seixeiro obtained an oncology certified nurse certification.

Presentations, Abstracts, and Publications
Anna Tobias, Cynthia Almonte, and Jamie Taratko presented “Driving Clinical Practice through the RN Champion Role” at the Oncology Nursing Society’s annual congress in April.

Addi Watters published “Complexity Is the Cornerstone of BMT Nursing” in ONS Voice on October 7.

Kelley Anderson and Mary Elizabeth Davis presented “The 1-2-3 Program: A Novel, Structured, Nurse-Driven Approach to the Promotion of Early Palliative Care in an Outpatient Cancer Clinic” at the Oncology Nursing Society’s annual congress in April.

Abigail Cohen and Emily Patterson presented “Nurse Practitioner (NP)-Led Intervention to Improve End-of-Life (EOL) Care for Critically Ill Bone Marrow Transplant Patients: Development and Implementation of a Goals-of-Care (GOC) Referral System” at the Oncology Nursing Society’s annual congress in April.

Selected Publications


MSK Is Recognized as an Employer of Excellence
The American Academy of Physician Assistants (AAPA) Center for Healthcare Leadership and Management (CHLM) honored Memorial Sloan Kettering with a 2019–2020 Employer of Excellence (EOE) Award at the AAPA’s 2019 conference in Denver. Heather Hylton, Director of Advanced Practice Providers, accepted the award on behalf of MSK.

“This is one of the most prestigious awards in the PA profession, and we truly celebrate this honor with immense gratitude for all of the support that has been provided along the journey,” says Ms. Hylton.

This is the first year that MSK has received this honor.

CHLM’s EOE Award is given to healthcare institutions that have created programs and tools that promote positive, engaging, and collaborative working environments. Recipients of the award are nominated by their PAs and recognized as model employers for current or potential PAs. MSK is one of 15 healthcare systems to win this year.
Pharmacy Publications, Presentations, and Recognition

Selected Publications


Poster Presentations

Presented at the American Society of Hematology (ASH) Annual Meeting, December 2019, Orlando, FL:

- King AC, Park JH, Geyer MB. Evaluation of Biomarkers as Predictors of Blinatumomab Toxicity and Real-World Management of Blinatumomab Toxicity in B-Acute Lymphoblastic Leukemia Patients.
- Yang X, Kabel CC, King AC. Park JH, Geyer MB. Inotuzumab Ozogamicin Is an Effective Salvage Therapy in Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia with High-Risk Molecular Features, Including TP53 Loss.
- Kabel CC, Goldman DA, Buie LW, Klimek VM. Choice of Hypomethylating Agent (HMA) for Initial Treatment Does Not Influence Outcome or Survival for Therapy-Related Myeloid Neoplasms (t-MN).

Presented at the Hematology/Oncology Pharmacy Association (HOPA) Annual Meeting; March 2019; Fort Worth, TX:


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National Presentations

- **Andrew Lin, PharmD, BCOP (BMT Service)**
  - Letermovir in Allogeneic Hematopoietic Cell Transplantation: Beyond the Labels. ORAL- ASBMT Transplantation and Cellular Therapy Meetings; Houston, Texas.

- **Carmen Lau, PharmD, BCOP (BMT Service)**

- **Tim Peterson, PharmD, BCOP (Multiple Myeloma Service)**
  - Lack of a Significant Pharmacokinetic Interaction between Letermovir and Calcineurin Inhibitors in Allogeneic HCT Recipients. ORAL- ASBMT Transplantation and Cellular Therapy Meetings; Houston, Texas.

- **Brianne Dixon, PharmD, BCOP (Lymphoma Service)**
  - APP Oncology Summit. Oncologic Emergencies. August 2019

- **Amber King, PharmD, BCOP (Leukemia Service)**
  - Management of BRAF inhibitor myalgias/arthritis. International Hairy Cell Leukemia Meeting. Rome, Italy. 2019

- **Charlene Kabel, PharmD, BCOP (Leukemia Service)**
  - Myeloproliferative Neoplasms (MPNs): Diagnosis, Treatment, and Side Effect Management - Leukemia & Lymphoma Society webinar presentation
  - Living Well with CLL: Diagnosis, Treatments, and Support – Leukemia & Lymphoma Society patient/caregiver education meeting

Awards and Honors

- **Carmen Lau, PharmD, BCOP (BMT Service)**
  - Best Abstracts, Second Place, at the TCT Pharmacists Conference at the American Society for Blood and Marrow Transplantation and Cellular Therapy Meetings, February 2019

National Committee Representation

- **Ryan Daley**
  - Committee member, Alliance for Clinical Trials in Oncology Pharmacy

- **Kathryn Maples**
  - Communications Working Committee member, American Society for Blood and Marrow Transplantation and Cellular Therapy's Pharmacy Special Interest Group
  - Membership Committee member, Hematology/Oncology Pharmacy Association

- **Valkal Bhatt**
  - Chair, Bone Marrow Transplant, Clinical Trials Network's Pharmacy Committee
  - Chair, International Society for Cell and Gene Therapy's Pharmacy Group of the APP and Pharmacy Special Interest Group
  - Communications Working Committee member, ASTCT's Pharmacy Special Interest Group

- **Brianne Dixon**
  - Fundraising Committee member, Lymphoma Research Foundation

- **Andrew Lin**
  - Communications Working Committee member, ASTCT's Pharmacy Special Interest Group

- **Andréa LeVoir**
  - Needs Assessment Committee member, Hematology/Oncology Pharmacy Association

- **Tim Peterson**
  - Abstract Review Committee member, Hematology/Oncology Pharmacy Association

- **Michael Buege**
  - Grant Review Committee member, Hematology/Oncology Pharmacy Association
MSK Cancer Alliance and the Division’s Engagement

The Memorial Sloan Kettering Cancer Alliance aims to bridge the divide between the cancer services offered by most community providers and MSK’s state-of-the-art cancer care. Currently, there are three member hospitals in the MSK Cancer Alliance: the Hartford HealthCare Cancer Institute in Connecticut, the Lehigh Valley Cancer Institute in Pennsylvania, and the Miami Cancer Institute at Baptist Health South Florida.

In 2019, MSK’s Bone Marrow Shared Care program with Hartford HealthCare continued to facilitate consultations and transplants. As of February 2020, the program referred 120 patients to MSK for a bone marrow transplant (BMT) consult; 50 of them ultimately received a transplant or cellular therapy. The clinical collaboration that fosters this program includes the alliance’s BMT liaison, MSK hematologic oncologist Craig Sauter, who virtually participates in Hartford HealthCare’s biweekly hematology case conferences. In that role, he provides opinions and guidance on patients who may be eligible for a transplant. The BMT Shared Care program effectively facilitates referrals and transplants for patients at MSK while allowing them to receive much of their pre- and post-transplant care in their local communities.

In addition, the BMT lecture series continued in 2019 and featured the following expert updates:

- **Raajit Rampal** spoke on myelofibrosis on January 28.
- **Heather Landau** spoke on amyloidosis on March 25.
- **Alison Moskowitz** and **Gunjan Shah** spoke about treating relapsed or refractory Hodgkin lymphoma on April 23.
- **Sergio Giralt** and **Ola Landgren** spoke about the upfront treatment of multiple myeloma on October 23.
- **Christian Grommes** and **Michael Scordo** presented on treatment for primary central nervous system lymphoma on October 23.
- **Richard Lin** spoke on transplant and cell therapy in older patients on November 25.

In 2019, MSK faculty also began participating virtually in hematology case conferences with the Lehigh Valley Cancer Institute. Participants included Drs. Sauter, Shah, and Moskowitz. Additionally, on September 12, **Anita Kumar** visited Lehigh Valley, where she participated in the case conference in person and discussed areas for collaboration.

In 2019, Marcel van den Brink visited the Miami Cancer Institute to give grand rounds. He met with colleagues there to discuss clinical research and additional opportunities for collaboration.

Also in conjunction with the MSK Cancer Alliance, Dr. Giralt and Steven Horwitz submitted two applications to the Leukemia and Lymphoma Society for its IMPACT grants. These grants are intended to expand access to high-quality clinical trials to people with blood cancers who are served by community healthcare organizations. Dr. Giralt’s project is entitled “Enhancing Access to Cellular Therapy Trials for Patients with Blood Cancers — Leveraging Modern Technology with Care Coordination,” and Dr. Horwitz’s project is entitled “Increasing Clinical Trial Access and Therapeutic Options for Patients with Uncommon Lymphomas.”

In 2019, Boglarka Gyurkocza’s observational study “Identify Barriers to Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Newly Diagnosed and Relapsed Acute Leukemia” opened at Lehigh Valley Cancer Institute. In addition, Eytan Stein’s study “A Biomarker-Directed Phase II Trial of SY-1425, a Selective Retinoic Acid Receptor Alpha Agonist, in Adult Patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)” opened at all three MSK Cancer Alliance member hospitals.
Memorial Sloan Kettering’s Hematologic Oncology Tissue Bank (HOTB) supports many research projects for Memorial Hospital and Sloan Kettering Institute investigators. The bank was founded by a Geoffrey Beene Cancer Research Center grant, the Division of Hematologic Malignancies, and the Sloan Kettering Institute in 2010.

Organized as a core laboratory at MSK, HOTB is a centralized, comprehensive resource for banking human biological specimens. It supports research using primary human cells and tissue. The facility provides appropriate cell and tissue-based specimens from people 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. Instead, they are cryopreserved in a manner that allows the recovery of viable cells. The bank also contains comparable materials from healthy volunteers, although these are more limited in quantity and scope.

When HOTB was created, it processed about 150 samples each month. Sample processing has steadily increased: currently, it processes between 2,000 and 2,500 samples per month. The current HOTB inventory comprises more than 355,000 aliquots, including peripheral blood components (plasma, serum, mononuclear cells, and granulocyte pellets for DNA), buccal swabs for DNA, bone marrow mononuclear cells, skin cells, and lymphoid tissue.

Research specimens are collected from the following services: Leukemia, Lymphoma, Multiple Myeloma, Adult Bone Marrow Transplant, Pediatrics, Developmental Therapeutics Center, Immunotherapeutics Core, and Dermatology. They are collected at sites in Manhattan as well as at MSK Regional Network sites.

In addition to tissue banking, HOTB supports specimen processing for more than 55 clinical trials within MSK. The samples from HOTB have facilitated research in exploring genetic mutations in cancer diagnoses, testing multiple mass spectrometry–based assays, xenograft profiling of hematologic malignancies, and many more areas.

Any MSK investigator with an Institutional Review Board–approved biospecimen research protocol may request samples, including investigators in Memorial Hospital, the Sloan Kettering Institute, and the Human Oncology and Pathogenesis Program.

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 people with lymphoid and hematologic malignancies.

**MSK Center for Hematologic Malignancies**

The Center for Hematologic Malignancies (CHM) serves people 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 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 collaboration. The retreat was attended by 120 CHM members and included formal talks and group discussions aimed at fostering new research directions and interactions. Keynote speaker Jonathan Licht, 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.

**Physician-scientist Ross Levine**
Fellowship Programs Train the Leaders of the Future

The Adult Hematopoietic Stem Cell Transplantation Fellowship Program and Parker Institute for 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 gaining experience with clinical research. The fellowship provides training in inpatient and outpatient settings, with a focus on the subspecialties within hematopoietic stem cell transplantation and cellular therapy, as well as exposure to the many 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 assignment of a mentor who ensures that the fellow’s objectives are met throughout the training year.

The program also includes a wide variety of conferences, which complement the clinical aspects. These are based on a disease-management concept and group 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 24 fellows. Twenty-one of the 24 graduates are now full-time faculty on blood and bone marrow transplant services at academic centers in the United States and abroad. One graduate is working as a senior director of clinical research at CRISPR Therapeutics. As of July 2019, the fellows’ research activities resulted in 42 publications.

In July 2018, a new fellowship in cancer immunotherapy was 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 MSK’s Adult Bone Marrow Transplant (BMT) Service, the Cellular Therapeutics Center at MSK, and the Parker Institute for Cancer Immunotherapy (PICI) at MSK and is supported by PICI. The clinical and research focus of the fellowship is on cellular therapy, including gene engineering and the use of immunotherapy approaches to cancer, including cancer vaccines and checkpoint inhibitors. The structure of the fellowship is similar to the BMT Fellowship, and fellows on the two tracks benefit from the premier training and research environment at MSK.


Urvi Shah, the first fellow selected for the Parker Institute for Cancer Immunotherapy Fellowship program and its first graduate, was recruited to the Myeloma Service in the Department of Medicine, joining as Assistant Member (Level 1) in April 2019.

Medical Oncology/Hematology Fellowship

Memorial Sloan Kettering’s Medical Oncology/Hematology Fellowship Training Program in the Department of Medicine has a tradition of developing the careers of leading physician-scientists by providing rigorous training in the diagnosis and treatment of neoplastic disorders as well as in the conduct of clinical and laboratory investigations. The 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 and 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 physicians, fellows must have a specific interest in clinical research or laboratory investigation and demonstrate scientific curiosity and motivation.

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

To learn more, visit www.mskcc.org/education/fellowships/fellowship/medical-oncology-hematology.
Parker Institute for Cancer Immunotherapy

Memorial Sloan Kettering is one of six founding centers of the Parker Institute for Cancer Immunotherapy (PICI). The goal of PICI is to accelerate the development of breakthrough immune therapies that are capable of turning most cancers into curable diseases by providing the resources (funding, immune-monitoring services, clinical trials management) and central coordination needed to advance research objectives, and by empowering scientists to pursue their boldest research ambitions.

The Parker Institute at MSK (PICI @ MSK) runs two internal competition programs to fund innovative, high-risk ideas related to cancer immunotherapy. Pilot Grants of $75,000 are provided as seed money to test novel hypotheses. The Career Development Awards grant $250,000 to young investigators. Since 2017, PICI @ MSK grant awardees have published 13 seminal research papers from their PICI-funded projects in high-profile journals, including:

- Marcel van den Brink and Jonathan Peled's publication in Science

- Alexander Lesokhin's publication in Blood Advances

- Alan Hanash's publications in *Immunity* and *Science Immunology*

In 2019, PICI @ MSK funded eight Pilot Grants, three of which were in the Division of Hematologic Malignancies.

**In July 2019, Kitsada Wudhikarn was selected as the second fellow of the Adult Cancer Immunotherapy Fellowship — PICI.**

**Attendees at the 2019 Parker Institute Parker Institute for Cancer Immunotherapy Scientific Symposium**
Initiated in 2010, the Susan and Peter Solomon Divisional Genomics Program at Memorial Sloan Kettering is a collaborative, multidisciplinary program comprised of clinical and research experts. Led by Marcel van den Brink, Ross Levine, and Elli Papaemmanuil, the program supports innovative discovery science and translation to the clinic, including the genomic profiling of MSK patients with leukemia. Genomic profiling has been used as the basis for mechanism-based clinical trials and has directly led to two clinical trials (of IDH2 and IDH1 inhibition) and the US Food and Drug Administration’s approval of an acute myeloid leukemia (AML) therapy: enasidenib (Idhifa®) for IDH2-mutant AML.

In 2019, the program began supporting Omar Abdel-Wahab and Michael Kharas on a project entitled “Understanding and Targeting Altered RNA Processing in Leukemia.” The goal is to provide new insights into dysregulated splicing and the altered RNA binding proteins (RBP) network in leukemia, which could lead to new therapeutic strategies.

We have continued to innovate and will soon begin combination therapy trials targeting multiple mutations in each patient, which wouldn’t be possible without the program’s support.
The tenth Annual Mortimer J. Lacher Lecture and Fellows Conference was hosted by the Division of Hematologic Malignancies on May 29, 2019. The event honors Dr. Lacher, a longtime member of the Lymphoma Service at Memorial Sloan Kettering, which he joined in 1960. He was a member of the Sloan Kettering Institute from 1960 until 1990. In 1965, he published a seminal report with John R. Durant describing the success of combining vinblastine and chlorambucil (Leukenar®) to treat Hodgkin’s disease.

Dr. Lacher is the co-founder and current president of the Lymphoma Foundation and a consultant to 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 lecture, “Progress and Challenges in Precision Therapy for B Cell Lymphoma,” was delivered by John Leonard, the Richard T. Silver Distinguished Professor of Hematology and Medical Oncology, the Senior Associate Dean for Innovation and Initiatives, and Executive Vice Chairman in the Department of Medicine at Weill Cornell Medicine. Dr. Leonard's primary research interests are in the development of novel therapeutic strategies for the treatment of lymphoma and related hematologic malignancies. Much of his work has involved the development of novel therapies for lymphoma, including monoclonal antibodies, other immune-based treatments, targeted agents, and other innovative approaches.

The 2019 Lacher Fellows are listed below along with their abstracts:

**Brian Ball**
Mentor: Eytan Stein
Overcoming RAS-Mediated Resistance to Targeted Therapies in AML

**Christopher Hackett**
Mentor: Renier Brentjens
Optimizing CAR T Cell Therapy for Lung Cancer

**Brandon Imber**
Mentor: Joachim Yahalom
Early Insights on Integrating Radiotherapy with CD19 Chimeric Antigen Receptor (CAR) T Cell Therapies for B Cell Lymphomas

**Niloufer Khan**
Mentor: Steven Horwitz
Optimizing Dosing of Brentuximab Vedotin for Cutaneous T Cell Lymphomas

**Lindsey Roeker**
Mentor: Anthony Mato
Chronic Lymphocytic Leukemia: Where We Are and Where We’re Going

**David Sermer**
Mentor: Renier Brentjens
CAR Models of the Past, Present, and Future

**Adam Widman**
Mentor: Omar Abdel-Wahab
Use of Whole-Genome Sequencing to Enable Highly Sensitive Liquid Biopsy for Early Cancer Detection

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From left: Marcel van den Brink, Christopher Hackett, Brandon Imber, Lindsey Roeker, John Leonard, Niloufer Khan, Adam Widman, David Sermer, and Brian Ball
Comedy vs Cancer

Comedy vs Cancer, a night of humor and hope to outwit blood cancer, raised more than $1 million for research at Memorial Sloan Kettering. There were roughly 1,000 people in the audience on Tuesday, May 14, 2019, at Jazz at Lincoln Center’s Frederick P. Rose Hall in New York City. Hosted by Nick Kroll, the all-star event featured comedians Hannibal Buress, Tina Fey, Jim Gaffigan, Jason Mantzoukas, Seth Meyers, John Mulaney, and Jaboukie Young-White. The show opened with a special surprise: a comedy routine from 8-year-old Audrey Lorenz, a blood cancer survivor who was diagnosed in 2017. Founders Nicole and Jeremy Kroll, Jennifer Rogers, and Robert Carlock, created the event as a unique and impactful way to fund cutting-edge blood cancer research at MSK, where Nicole and Jennifer were treated years ago.

Comedians who performed at the event (from left): Jason Mantzoukas, Tina Fey, Jaboukie Young-White, Nick Kroll, Seth Meyers, and Jim Gaffigan

Comedy vs Cancer grant awardees in 2019

Eric Smith
Micropharmacy CAR T cells secreting IL-15 and scFv-Fc engage innate and adaptive immunity to enhance the efficacy of adoptive cellular therapy for multiple myeloma

Scott James
Multiantigen-specific CAR T cells to treat acute myeloid leukemia

Prasad Adusumilli
IL-7 receptor-targeted chimeric antigen receptor T cell therapy for T cell acute lymphoblastic leukemia: preclinical evaluation and clinical trial preparation

Anthony Daniyan
Targeting AML with CD371-directed chimeric antigen receptor T cells and chemo/immunotherapy

Kevin Curran
Off-the-shelf CAR T cells for adult/pediatric hematologic malignancies

Brandon Imber
A pilot, proof-of-principle clinical trial of bridging radiotherapy prior to commercial CD19 CAR T therapies for patients with relapsed or refractory B cell malignancies

Michael Scordo
Personalizing CAR T cell conditioning regimens to optimize survival and mitigate toxicities

Mark Geyer
Iomab-ACT: a phase I/II study of iomab-b followed by CD19-targeted CAR T cell therapy for patients with relapsed or refractory B cell acute lymphoblastic leukemia or diffuse large B cell lymphoma

Bianca Santomasso
A longitudinal neuroimaging and neurocognitive study in lymphoma patients treated with CD19 CAR T cell therapy
Fred’s Team

Fred’s Team, named after running legend 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 fundraise to further MSK’s pioneering research and support the Aubrey Fund for Pediatric Cancer Research.

The Aubrey Fund, named after Fred’s Team runner and pediatric cancer survivor Aubrey Barr, provides essential support for groundbreaking therapies, advanced research, and next-generation cancer treatments.

More than 900 Fred’s Team members took part in the 49th New York City Marathon on November 3, 2019, and raised nearly $6.3 million. In total, Fred’s Team has raised more than $88 million since 1995.

www.fredsteam.org

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 $85 million to fund cancer research and clinical trials at world-renowned organizations.

Today, more than 5,000 recreational swimmers, master swimmers, and even kayakers and boaters participate in 21 open-water swimming fundraising events and more than 100 pool fundraisers.

James Young, Attending Physician in Memorial Sloan Kettering’s Adult Bone Marrow Transplant (BMT) Service and an avid distance swimmer, began swimming the Long Island Sound Open Water Swim in 2006 and founded Team Transplant in 2008 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 2019, Team Transplant participated in its 11th consecutive swim at the SAA Long Island Sound Open Water Swim and raised $21,500. Since 2009, Team Transplant has raised $235,000 for much-needed support of the 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.

www.swimacrossamerica.org
Cycle for Survival

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

Cycle for Survival is determined to beat rare cancers by powering research that helps patients who often have few or no options. With support from our founding partner Equinox, Cycle for Survival had its biggest fundraising year in 2019. Raising $42 million — and more than $220 million during the past 13 years — was only possible because of our dedicated community of riders, supporters, patients, researchers, and doctors. Some 36,000 people across 16 cities participated in the event in 2019, more than 2,100 of whom were Memorial Sloan Kettering employees. Within six months of the annual event, all money raised went directly to groundbreaking research. Every dollar empowers researchers to pursue revolutionary ideas that lead to lifesaving breakthroughs. We are proud to support the advancement of several comprehensive initiatives at MSK, which span many critical areas of research. MSK is on the front line of the battle against rare cancers.

Members from the division participated in the following teams:

1. The CanCer HaCkers
2. Dean’s Cell Cyclers
3. DoMinators
4. Straight Outta Chemo
5. The Mobilizers
6. The Nutcrackers
7. Team HOPP Kreb’s Cycle
8. Lowe Riders
9. MSK BMT Cyclepaths
10. BMT Cancer Crushers

www.cycleforsurvival.org
Philanthropic Donors
Over $50,000

The Division of Hematologic Malignancies is supported in part by the generous donations of our benefactors.

We wish to thank those who have contributed to the many successes of the division.

Below is a list of patrons who donated $50,000 or more in 2019.

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The American-Italian Cancer Foundation
The American Society of Hematology
The Aplastic Anemia and MDS International Foundation
Joyce Ashley
The David R. and Patricia D. Atkinson Foundation
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GIVING
There are so many ways your dollars can drive cancer research and treatment at Memorial Sloan Kettering Cancer Center.

For additional information or to make a gift, call 866-815-9501 or visit giving.mskcc.org.

DONATING BLOOD
Blood donations can be designated for a particular patient or MSK’s general blood inventory.

For more information or to make an appointment, call 212-639-8177 or 212-639-7648.

DONATING TO FRED’S TEAM
For information on donating to Fred’s Team, visit: www.fredsteam.org.

DONATING TO CYCLE FOR SURVIVAL
For information on donating to Cycle for Survival, visit: www.cycleforsurvival.org.