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An Unwanted Companion to Transplant Medicine: Post-transplant Lymphoproliferative Disorder

Post-transplant lymphoproliferative disorder (PTLD) is a cruel companion to both solid organ transplantation and hematopoietic stem cell transplant in both pediatric and adult patients. With the steadily increasing numbers of transplants occurring in pediatric patients in the United States each year, the incidence of PTLD is also increasing. The risk for PTLD in solid organ transplant is anywhere from 2 to 15 percent, with percentages varying based on the organ or organs and other factors.

Because of its expertise and success with transplant medicine as a whole, UPMC Children's Hospital of Pittsburgh has high annual volumes of pediatric transplants and so sees and treats transplant patients with PTLD more so than many other centers.



"Small bowel transplants have the highest incidence of PTLD, likely because of the relatively higher immunogenic nature of the organ when compared to the liver, for example. UPMC

Children's transplant program for small bowel is one of the largest in the United States.

Therefore, we treat PTLD patients frequently and have a number of protocols and trials in progress that guide our care while we work to find new, better therapies to combat the condition," says **Erika Friehling, MD**, assistant professor of pediatrics and fellowship program director in the Division of Pediatric Hematology/Oncology.

Dr. Friehling joined the Division of Pediatric Hematology/Oncology as a faculty member in 2013 after completing her fellowship training at UPMC Children's under the supervision of A. Kim Ritchey, MD.

A 2015 recipient of the American Society of Pediatric Hematology/Oncology Clinician Educator Award, Dr. Friehling devotes a great deal of her time to educating residents and fellows, and she has a special interest in PTLD from both a research and clinical care perspective, having authored several recent papers on the subject.

PTLD Risk Factors

While PTLD can occur with any solid organ transplant, and while small bowel incidence is higher than other organs, a full 90 percent of all cases are of the Epstein-Barr virus (EBV) positive, CD20-positive variety. "Most cases of PTLD are EBV-driven," says Dr. Friehling. Under normal circumstances, EBV infection would likely be of no consequence. However, in transplant patients who are on immunosuppressive regimens to prevent organ rejection, the immunosuppression itself is a risk factor.

Another potential risk factor appears to be age. A younger patient's native immune system is relatively more naïve than that of older

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patients, and this might predispose younger transplant patients to acquire PTLD. The evidence is not firm yet on this aspect of PTLD, but researchers are actively pursuing a better understanding of this potential pathway to disease.

The Clinical Conundrum of Immunosuppression and Treating PTLD

Cases of PTLD can be curable, but it becomes a delicate balance in treating these patients because of the need for immunosuppression to preserve transplant organ function. “The importance of a collaborative approach to disease management is highlighted by cases of PTLD. Moreover, it matters which organs are involved for optimal management. If PTLD arises in a liver transplant patient, we can typically decrease immune suppression for a time to combat the PTLD without the likelihood of immediate organ rejection. However, heart transplant patients are entirely different. Stopping immune suppression

can lead to organ rejection and potentially life-threatening complications. The approach to care is incredibly nuanced. We have cases that require almost daily modification of the care plan, balancing the needs for immunosuppression and treatments for lymphoma simultaneously. It is a challenging and complex set of circumstances,” says Dr. Friehling.

Clinical Trials in Progress

UPMC Children’s is one of approximately 25 centers in the United States participating in a clinical trial that is investigating the use of rituximab in combination with cytotoxic T-lymphocyte grafts of latent membrane protein (LMP)-specific T cells to combat PTLD in pediatric solid organ transplant patients.

The trial, which is currently recruiting patients, is sponsored by the Children’s Oncology Group and the National Cancer Institute. Patients must have EBV-positive, CD-20 positive cases of PTLD to qualify for enrollment.

The importance of a collaborative approach to disease management is highlighted by cases of PTLD. Moreover, it matters which organs are involved for optimal management.

“Once enrolled in the trial, patients will first receive a three-week regimen of rituximab immunotherapy. At the end of the first three weeks, if the PTLD has improved, they will continue receiving rituximab. However, if at the end of the first three weeks the PTLD has not improved, they are eligible to receive the LMP-specific T cell infusions,” says Dr. Friehling.

For complete study details and protocols, please visit [ClinicalTrials.gov](https://clinicaltrials.gov) and search under trial number NCT02900976.

Further Reading

More of Dr. Friehling’s research into PTLD can be found in the following published papers.

Epperly R, Ozolek J, Soltys K, Cohen D, Rakesh G, Friehling E. Treatment of Pediatric Plasma Cell Myeloma Type Post-transplant Lymphoproliferative Disorder With Modern Risk-Directed Therapy. *Pediatr Blood Cancer*. 2018 Oct; 65(10): e27283.

Stanley K, Friehling E, Ranganathan S, Mazariogos G, McAllister-Lucas LM, Sindhi R. Post-transplant Lymphoproliferative Disorder in Pediatric Intestinal Transplant Recipients: A Literature Review. *Pediatr Transplant*. 2018. Aug; 22(5) e13211.

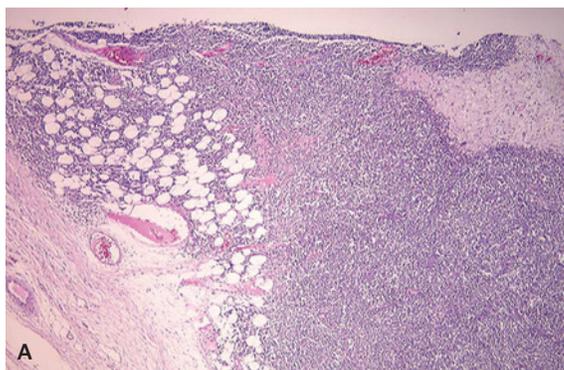
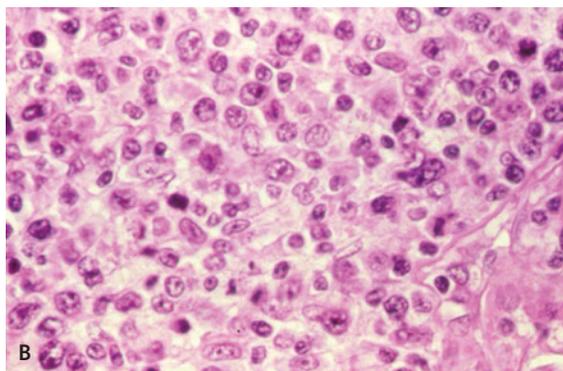


Figure A: PTLD infiltrate involving perirenal fat (left). A small area of necrosis appears as a pink area in the upper right hand portion. (Courtesy of UPMC Transplant Pathology Internet Services.)

Figure B: Polymorphous PTLD with the entire spectrum of lymphoid differentiation represented in the lesion. (Courtesy of UPMC Transplant Pathology Internet Services.)



New Clinical Trials in Crohn's Disease, Systemic Sclerosis, Sickle Cell Disease, and Tandem Lung/BMT Transplant

The Division of Blood and Marrow Transplantation and Cellular Therapies (BMT-CT), led by **Paul Szabolcs, MD**, Division chief and professor of Pediatrics and Immunology at the University of Pittsburgh School of Medicine, places special emphasis on the development and use of reduced-intensity/toxicity transplant regimens for a range of non-malignant conditions.



Historically, these have been applied to inborn errors of immunity and inherited metabolic disorders such as mucopolysaccharidosis syndromes (MPS) and leukodystrophies. In fact,

the Division is submitting data for publication reporting on their prospective trial outcome that shows ~ 95% survival at the critical one-year valuation point — even with unrelated donor cord blood or bone marrow grafts (ClinicalTrials.gov NCT01962415) — which is unsurpassed anywhere.

Clinical research within the Division has led to new trial designs that recently have been approved by the U.S. Food and Drug Administration (FDA) and Institutional Review Board (IRB) of the University of Pittsburgh to bring a cure or alleviate advanced cases of certain autoimmune disorders such as Crohn's disease (CD) and systemic sclerosis (SSc). Another exciting new protocol also received FDA and IRB approval, whereby all sickle cell disease (SCD) patients who may benefit from allogeneic transplant would be able to find partially matched healthy unrelated stem cell donors.

Toward these objectives, the BMT-CT Division is collaborating with pediatric and adult gastroenterology, rheumatology, cardiology, and pulmonary specialists from UPMC and the University of Pittsburgh, to form CD, SSc, and SCD disease-specific task forces led by Dr. Szabolcs. Pediatric and adult candidates who have traveled from distant locations in the United States are already being screened and treated. UPMC Children's Hospital of Pittsburgh is the only entity in the world currently performing tandem cadaveric lung and bone marrow transplantation for both

pediatric and adult patients diagnosed with a primary immunodeficiency with progression to end-stage lung disease. Early favorable experience has now led to new indications that are focusing first on combined bone marrow and lung failure related to a diagnosis of idiopathic pulmonary fibrosis.

Collaborating With the New UPMC Immune Transplant and Therapy Center

In February 2018, UPMC and the University of Pittsburgh announced the establishment of the UPMC Immune Transplant and Therapy Center (ITTC), a bold and ambitious effort to revolutionize the way the world thinks about — and treats — a variety of diseases and conditions. ITTC brings together immunotherapy and transplant researchers in the areas of cancer, organ transplantation, and aging to collaborate, share ideas, and drive further development in this promising new frontier of medicine.

Dr. Szabolcs has joined ITTC as part of its transplant program, and will be working to continue his research and clinical trials into various aspects of immunotherapy and blood and marrow transplantation. The first trials Dr. Szabolcs will conduct through ITTC are a modification to his existing autologous stem cell transplant protocol for Crohn's disease, and new trials focused on tandem lung/BMT transplant, systemic sclerosis, and sickle cell disease.

"We hope to make a significant impact in terms of outcomes, both for proving immune transplantation as a safer than previously believed technology and for making it more effective, either as a complete cure or at least by providing a significant improvement in quality of life or number of diseases. For some conditions, like sickle cell disease,

immune transplantation can be curative by replacing the faulty hematopoietic system with a healthy one. For other conditions, for example, autoimmune diseases, we could achieve a new steady-state of disease where the patient's immune system is no longer eroding and attacking their tissues, be it the lungs, intestines, or skin," says Dr. Szabolcs.

New Tandem Lung and BMT Transplant Trial

Building off of an in-progress, NIH-funded clinical trial to perform cadaveric bilateral orthotopic lung transplantation followed by sequential bone marrow transplantation for patients with primary immunodeficiency and end-stage lung disease with study collaborator John McDyer, MD, associate professor in the Division of Pulmonary, Allergy, and Critical Care Medicine, and director of the Lung Transplantation Translational Research Program, Dr. Szabolcs and team recently received IRB and FDA approval for a second, similar trial that will study the effects of tandem lung and bone marrow transplant in patients with combined lung and bone marrow failure. The goal of this study is to correct the patient's bone marrow failure and potentially help to build tolerance to the transplanted lungs, thus eliminating the need for lifelong immunosuppression while improving quality of life. In the new trial through ITTC, Dr. Szabolcs hopes to perform lung transplantation for patients with idiopathic pulmonary fibrosis or COPD/emphysema, followed by a bone marrow transplantation protocol designed by Dr. Szabolcs.

"The BMT and conditioning therapy for this trial is tailored for the specific pathology and also comorbidities of this patient population.

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Supportive Care at UPMC Children's

The Supportive Care Program at UPMC Children's Hospital of Pittsburgh has a long history of supporting pediatric patients and their families who are facing serious, life-limiting or life-threatening conditions — be they acute or chronic. This support also extends to the providers and staff throughout the hospital who work around the clock to care for these patients. And since its inception 15 years ago — in 2003 — the Supportive Care Program has had the unwavering support of hospital administration and leadership.



Carol May, RN, MSN, MBA, CHPPN, has been the program manager since its inception, having been recruited to work to develop it a decade and a half ago. "Dr. Eugene

Wiener who was, at the time, our medical director and surgeon-in-chief had some exposure to supportive and palliative care and it was his hope that we would institute a program at UPMC Children's," explains Ms. May.



Since its early days, the program has expanded in scope and practice and routinely sees patients from virtually every division within the hospital.

Scott Maurer, MD, joined the program as one of its

physicians in 2010. "Within the hospital, our largest referral source is probably from the neonatal intensive care unit, followed by cardiology and oncology, but we really do get consults from just about everywhere — nephrology, GI, neurology, and others," says Dr. Maurer.

The program boasts a full-time bereavement coordinator who manages follow-up with all families who have lost a child in the hospital or at home. Part of this bereavement care is a 13-month close follow-up program which includes the ability to direct people to resources and grief support groups. Mailings and cards also are sent at certain times of the year to families.

In 2017, the Supportive Care Program launched Camp Wakchazi, a four-day sibling bereavement camp designed to help young children and adolescents who have

experienced the loss of a sibling. The 2018 camp held in June saw more than half of the participants returning from the previous year because of the support they receive from the peer counselors and the other campers.

Training and Education Initiatives

Formalized training and education for providers on the role and benefits of supportive care has been a part of the Support Care Program's mission since its inception. The majority of pediatric residents rotate with the program from anywhere from one to four weeks.

"We focus a lot of our teaching on pain and symptom management, but also on critical communication skills. This goes way beyond just how to approach end-of-life conversations," says Dr. Maurer, who also spends a significant amount of time giving lectures and holding discussion groups with both students and colleagues throughout the hospital.

Ms. May coordinates ongoing education and lectures for nursing staff and other providers. "A lot of what we do is informal, one-on-one discussions that tend to tackle specific problems or cases. We provide a level of support to the clinical staff who are dealing with these often complex and difficult situations both in terms of patient and family care, but with themselves and how they are handling these and the emotions that can arise," says Ms. May.

For the last seven years, the Supportive Care Program has conducted at one-day supportive and palliative care conference for providers. Typically offered during the month of May, the conference features a range of topics and speakers from the Supportive Care Program at UPMC Children's and the Section of Palliative Care and Medical Ethics at the University of Pittsburgh.

Community Outreach

Education and assistance do not stop at the front door of UPMC Children's. Because patients are often referred to outside sources for things such as hospice or home care, Ms. May and her team are continually active in discussions and education with numerous outside groups and agencies.

"Many times, we will have hospice organizations that are primarily taking care of adult patients come in to discuss and learn more about working with children and their families. Children are a much different set of patients than adults with respect to supportive care and have special needs that must be attended to. We make ourselves available to consult whenever they need us, after hours or otherwise. We want them to contact us when they need help or need to confer on a challenging aspect of patient care," says Ms. May.

Telemedicine Adoption

The adoption and spread of telemedicine across medical disciplines continues. It has also come to the Supportive Care Program at UPMC Children's through the help of a grant secured by Ms. May and her colleagues. Support and follow-up via phone has always been an integral part of the program. The recent grant has allowed for the purchase of tablet devices and a HIPAA-compliant secure connection through the hospital to provide care to patients at home. "Children want to be at home and we want them to be at home," says Dr. Maurer, "Carol fields the phone calls and works diligently to provide the support the family needs. We have been successful over the years at avoiding countless visits to the emergency department through our

work. Telemedicine and its reach will help us to continue this trend.”

Research

The incredible amount of research being conducted at UPMC Children’s across disciplines is one of the reasons it is consistently mentioned as a leading children’s hospital in the United States and internationally. This legacy of research is also part of the Supportive Care Program, one that continues to grow. Dr. Maurer explains that a new clinical investigator will be joining the system who has a special interest in quality-of-life issues for medically complex pediatric patients, a largely untapped research area in the field.

The program also is part of a large multi-center consortium working to better understand how pediatric patients progress through complex medical therapies for conditions such as cancer. “This study is unique in that the patients are able to report on their own adverse effects of chemotherapy. UPMC Children’s is one of the highest enrolling sites in this study at the moment. Ultimately, it’s a way to try and give these patients a voice in their own cancer care,” says Dr. Maurer.

Future Plans and Growth Opportunities

There’s much on the horizon for the Supportive Care Program. “We’re already a busy practice with typically 40 inpatient visits a day, and more than 200 patients on our service at any given time, but we can do more,” says Ms. May.

There are plans to grow the bereavement program to support more children and families in the community with a longer follow-up period of two years. It is well documented in the literature that the experience of grief and loss and its accompanying issues are actually more prevalent in the second year after the loss of a child or sibling.

There also exists the desire to better reach and service the cystic fibrosis patient population with earlier involvement and assistance with advance care planning, symptom management, and the transition to adult care. “As we see more children living longer with complex, chronic illnesses who 20 years ago may not have survived into adulthood, we need to progress as a discipline to meet their evolving needs, and we need to help our colleagues do so as well. These transitions in care are critically important for everyone involved, and our work and research to facilitate,

educate, and provide the best care possible in these circumstances will be a large focus for our team and program well in to the future,” says Dr. Maurer.

References and Further Reading

For more information about the Supportive Care Program at UPMC Children’s, please visit CHP.edu/SupportiveCare.

Supportive Care Program Team

Scott H. Maurer, MD – *Medical Director*

Carol May, RN, MSN, MBA, CHPPN – *Program Manager*

Alyssa Baker, PA-C

Amanda Brown, MD

Alicia Kolling, PA-C

Lori Malazich, LCSW – *Bereavement Coordinator*

Heather Morgan, PA-C

Justin Yu, MD

Recent Publications

McAuley JR, Freeman TJ, Ekambaram P, Lucas PC, McAllister-Lucas LM. CARMA3 Is a Critical Mediator of G Protein-Coupled Receptor and Receptor Tyrosine Kinase-Driven Solid Tumor Pathogenesis. *Front Immunol*. 2018; 9: 19887. Epub ahead of print.

DeRenzo C, Lam C, Rodriguez-Galindo C, Rapkin L, Gottchalk S, Venkatramani R. Salvage Regimens for Pediatric Patients With Relapsed Nasopharyngeal Carcinoma. *Pediatr Blood Cancer*. 2019 Jan; 66(1): e27469.

Nolfi-Donagan D, Konar M, Vianzon V, MacNeil J, Cooper J, Lurie P, Sedivy J, Wang X, Granoff DM, McNamara L. Fatal Nongroupable Neisseria meningitidis Disease in Vaccinated Patient Receiving Eculizumab. *Emerg Infect Dis*. 2018 Aug; 24(8). Epub ahead of print.

Nugent BD, Bender CM, Sereika SM, Tersak JM, Rosenzweig M. Cognitive and Occupational Function in Survivors of Adolescent Cancer. *J Adolesc Young Adult Oncol*. 2018; 7(1): 79-87.

Cashell J, Smink GM, Helm K, Xavier F. Kaposiform Hemangioendothelioma With Kasabach-Merritt Phenomenon in an Infant: Successful Treatment With Prednisone, Vincristine, and Addition of Sirolimus. *Pediatr Blood Cancer*. 2018 Dec; 65(12): e27305.

Dolezal JM, Dash AP, Prochownik EV. Diagnostic and Prognostic Implications of Ribosomal Protein Transcript Expression Patterns in Human Cancers. *BMC Cancer*. 2018 Mar 12; 18(1): 275.

Wang H, Dolezal JM, Kulkarni S, Lu J, Mandel J, Alencastro F, Duncan AW, Prochownik EV. Myc and ChREBP Cooperatively Regulate Normal and Neoplastic Hepatocyte Proliferation. *J Biol Chem*. 2018; 293: 14740-14757.

Gu L, Zhu Y, Lin X, Li Y, Cui K, Prochownik EV, Li Y. Amplification of Glyceronephosphate O-Acyltransferase and Recruitment of USP30 Stabilize DRP1 to Promote Hepatocarcinogenesis. *Cancer Res*. 2018; 78: 5808-5819.

Goetzman ES, Prochownik EV. The Role For Myc in Coordinating Glycolysis, Oxidative Phosphorylation, Glutaminolysis, and Fatty Acid Metabolism in Normal and Neoplastic Tissues. *Front Endocrinol (Lausanne)*. 2018 Apr 12; 9: 129.

Meenan C, Kelly J, Wang L, Ritchey A, Maurer S. Obesity in Pediatric Patients With Acute Lymphoblastic Leukemia Increases the Risk of Adverse Events During Pre-Maintenance Chemotherapy. *Pediatr Blood Cancer*. 2018. e27515.

Trauernicht E, Bharil S, Panko L, Friehling E. Fever, Neck Pain, and Back Pain in a 16-year-old Boy. *Pediatrics in Review*. 2018; 39(9): 468-469.

Epperly R, Ozolek J, Soltys K, Cohen D, Goyal R, Friehling E. Treatment of Pediatric Plasma Cell Myeloma Type Post-transplant Lymphoproliferative Disorder with Modern Risk-Directed Therapy. *Pediatric Blood & Cancer*. 2018; 65(10): e27283.

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About the Divisions

Division of Pediatric Hematology/Oncology



Under the leadership of **Linda M. McAllister-Lucas, MD, PhD**, division chief and associate professor of Pediatrics at the University of Pittsburgh School of

Medicine, UPMC Children's Hospital of Pittsburgh Division of Pediatric Hematology/Oncology boasts the largest and most comprehensive care center in western Pennsylvania, eastern Ohio, and northern West Virginia for pediatric and young adult patients with all forms of cancer and disorders of the blood. The Division is part of UPMC Hillman Cancer Center.

Research and Clinical Trials

The Division supports an extensive research program of basic science, translational investigations, and clinical trials. This work is collectively dedicated to uncovering new insights and knowledge with respect to how

Clinical Programs and Services

- Adolescent and Young Adult Oncology
- Pediatric Solid Tumors
- Hemophilia
- Hemostasis and Thrombosis
- Leukemia
- Sickle Cell Disease
- Neuro-Oncology
- Pediatric Cancer Survivorship Clinic
- Mario Lemieux Lymphoma Center for Children and Young Adults
- Cancer Predisposition Program
- Bone Marrow Failure
- Immunocytopenias
- Melanoma

and why cancers develop and spread, and to developing the next generation of therapies.

Division of Blood and Marrow Transplantation and Cellular Therapies



The Division's clinical efforts are focused on designing and testing transplant therapies for patients with leukemia, lymphoma, and other malignancies, as well as nonmalignant immune deficiencies, autoimmune conditions, and various neurodegenerative conditions.

Led by **Paul Szabolcs, MD**, division chief, and professor of Pediatrics at the University of Pittsburgh School of Medicine, the division places special emphasis on the development and use of reduced-intensity/ toxicity transplant regimens for a range of conditions related to mucopolysaccharidoses, leukodystrophies, and other inherited metabolic disorders.

Clinical research within the division spans a range of autoimmune disorders, cancers of the blood, and such conditions as sickle cell disease. Crohn's disease is of particular research interest, with several ongoing phase 1 and phase 2 clinical trials investigating the efficacy of autologous stem cell transplantation in tandem with high-dose chemotherapy.

At present, the division, in collaboration with investigators and surgeons from UPMC and the University of Pittsburgh, is the only entity in the world currently performing lung and bone marrow transplantation in tandem for both pediatric and adult patients who have immunodeficiencies with progression to pulmonary failure.

Division News and Updates

New Faculty Members

Joining the Division of Pediatric Hematology/Oncology in 2018 were **James Felker, MD**; **Ramasubramanian Kalpatthi, MD, FAAP**; **Julia Meade, MD**; and **Deirdre Nolfi-Donagan, MD**.

Faculty Accomplishments and Awards

Cheryl Hillery, MD, was selected to join the editorial board of the journal *Blood Advances*.

A. Kim Ritchey, MD, was selected for the honorary "Alan Coopersmith Visiting Professorship" at Johns Hopkins University for the 2018 academic year.

Speaking Engagement and Presentations

Edward Prochownik, MD, PhD, was an invited speaker at an NIH workshop titled "Frontiers in Targeting Myc."

Scott Maurer, MD, gave a platform presentation at the Religion and Medicine Annual Conference in St. Louis, Missouri. Dr. Maurer's presentation was titled "Religion, Spirituality and Medicine: Impact of an Educational Intervention for Medical Students and Physicians."

Erika Friehling, MD, led the "Leadership Skills" workshop at the Association of Pediatric Program Directors meeting in Philadelphia, Pennsylvania.

Andrew Bukowski, MD, was invited to present the ADVL1512 study at the CTEP Early Drug Development Conference in Bethesda, Maryland.

New Grants and Research Funding

Linda McAllister-Lucas, MD, PhD, received a \$2.5 million grant from the NIH/NCI for work on "New Mechanisms for Modulating the MALT1 Oncoprotein."

Ram Kalpatthi, MD, FAAP, received two new pilot grant awards for clinical research. The first is for an investigation on "Novel Biomarker of Neurocognitive Function in Children and Adults With Sickle Cell Disease." The second grant will examine "Contrast Enhanced Ultrasonography Study of Cerebral Blood Flow Velocity in Sickle Cell Disease."

Crohn's Disease and Tandem Lung/BMT Transplant *(Continued from Page 3)*

The radiation is a bit more intense than in our other trial, but we will be using more shielding to other organs and the chemotherapy aspect is scaled down," says Dr. Szabolcs.

This study protocol focuses on performing combined transplantation for candidates who are unable to undergo a standard lung transplant. Lung transplantation followed by BMT would allow for restoration of pulmonary and hematologic function post-BMT transplantation.

The secondary objectives of the trial are to evaluate the feasibility and long-term complications associated with combined solid organ transplant and BMT, including the ability to initiate and successfully withdraw participants from immunosuppression following BMT and attain independence from growth factors and red blood cell or platelet transfusions. This first-in-human pilot study hopes to enroll eight participants between the ages of 18 and 60 and is expected to be completed in 2026.

Autologous Stem Cell Transplant Trial for Crohn's Disease

Dr. Szabolcs and collaborators have modified an existing autologous stem cell transplant protocol for Crohn's disease (started in 2012 at UPMC Children's) to provide a safer and anticipated more effective conditioning regimen for these patients. The protocol for the trial includes a high-dose chemotherapy

conditioning regimen followed by a stem cell transplant consisting of a CD34-selected graft, <https://clinicaltrials.gov/ct2/show/NCT00692939>.

This trial is based out of UPMC Children's, with assistance from UPMC Presbyterian for adult patients, and is targeted at individuals between the ages of 10 and 60.

"We performed the first proof-of-principle transplant with the new protocol in December 2017. At present, we are at the end of our 12-month evaluation process and the patient is doing dramatically better. We are now enrolling the next subjects, most of whom are middle-aged adults," says Dr. Szabolcs.

Systemic Sclerosis — New Clinical Trial

The trial, "Autologous Stem Cell Transplantation with CD34-Selected Peripheral Blood Stem Cells (PBSC) in Patients with Treatment-Resistant Systemic Sclerosis (SSc)," utilizes low doses of radiation paired with more intense immunoablative serotherapy in preparation for an autologous CD34-selected stem cell transplant for patients diagnosed with systemic sclerosis.

"We hypothesize that this conditioning regimen, followed by an autologous stem cell transplant, is a safer method compared to other centers with more aggressive conditioning regimens that will possibly delay disease recurrence or progression," says Dr. Szabolcs.

This study is open to children and adults between the ages of 16 and 70. For additional requirements and criteria, please visit <https://clinicaltrials.gov/ct2/show/NCT03630211>.

Sickle Cell Disease Study

This trial, led by principal investigator Beth Carella, DO, also from the BMT-CT Division, is named "T-Cell Depleted, Alternative Donor Transplant in Pediatric and Adult Patients with Severe Sickle Cell Disease (SCD) and Other Transfusion-Dependent Anemias." Drs. Szabolcs and Carella collaborated with SCD specialists from both adult and pediatric hematology in the development of this trial.

This reduced intensity, immunoablative conditioning regimen is expected to prevent severe graft-versus-host disease by T-cell depletion, while at the same time minimizing the possibility of immune rejection in patients with sickle cell disease and other transfusion-dependent anemias such as beta-thalassemia or Diamond-Blackfan anemia. If successful, participants in this trial should achieve sufficient engraftment to allow for their disease-related symptoms and quality of life to improve.

This study is open to children and adults between the ages of 5 and 40. For additional requirements and criteria, please visit <https://clinicaltrials.gov/ct2/show/NCT03653338>.

Recent Publications *(Continued from Page 5)*

Stanley K, Friehling E, Davis A, Ranganathan S. SDH-Deficient GIST with SDHC Germline Mutation and Bilateral Renal and Neck Cysts. *Pediatric and Developmental Pathology*. 2018; Accepted, in press.

Stanley K, Cooper JD. Hormone Therapy and Venous Thromboembolism in a Transgender Adolescent. *J Pediatr Hematol Oncol*. 2018 Jan; 40(1): e38-e40.

McCormick MC, Siripong N, Cooper JD. Desmopressin Stimulation Testing: Response to Intravenous and Intranasal Forms. *Haemophilia*. 2018 Mar 26; ePub ahead of print.

Nolfi-Donagan D, Konar M, Vianzon V, MacNeil J, Cooper JD, Lurie P, Sedivy J, Wang X, Granoff DM, McNamara L. Fatal Nongroupable Neisseria

Meningitidis Disease in Vaccinated Patient Receiving Eculizumab. *Emerg Infect Dis*. 2018 Aug; 24(8): 1561-1564.

Close A, Sequeira G, Alessi L, Montano G, McCormick MC, Cooper JD, Epperly R, Zuckerbrun N. Improving the Evaluation and Management of Abnormal Uterine Bleeding in Adolescent Females Presenting to Emergency Care. *J Adolescent Gynecology*. Accepted for publication.

Pinto EM, Hamideh D, Bahrami A, Orr BA, Lin T, Pounds S, Zambetti GP, Pappo AS, Gajjar A, Agnihotri S, Broniscer A. Malignant Rhabdoid Tumors Originating Within and Outside the Central Nervous System are Clinically and Molecularly Heterogeneous. *Acta Neuropathol*. 2018; 136: 315-326.

Broniscer A, Jia S, Mandrell B, Hamideh D, Huang J, Onar-Thomas A, Gajjar A, Raimondi SC, Tatevossian RG, Stewart CF. Phase 1 Trial, Pharmacokinetics, and Pharmacodynamics of Dasatinib Combined With Crizotinib in Children With Recurrent or Progressive High-grade and Diffuse Intrinsic Pontine Glioma. *Pediatr Blood Cancer*. 2017; Epub ahead of print.

Upadhyaya SA, R McGee, Wilky B, Broniscer A. Malignant Progression of a Peripheral Nerve Sheath Tumor in the Setting of Rhabdoid Tumor Predisposition Syndrome. *Pediatr Blood Cancer*. Epub ahead of print. DOI: 10.1002/pbc.27030.

UPMC Physician Resources

CME, News, Events for Physicians from UPMC

Publications, free continuing medical education, and other resources are available by visiting UPMCPhysicianResources.com/PedsCancer. Below is a sample of the current CME courses in hematology/oncology.

Adolescent and Young Adult Cancer Treatment



Presented by: Louis Rapkin, MD, Clinical Director, Oncology, UPMC Children's Hospital of Pittsburgh

Louis Rapkin, MD, gives a presentation on cancer incidence in children and young adults. Dr. Rapkin also covers trends in cancer treatments and unique issues.

Hot Topics in Pediatric Hematology and Oncology



Presented by: A. Kim Ritchey, MD

Dr. Ritchey discusses hemophilia treatment options, T-cell directed therapy for relapsed acute lymphoblastic leukemia (ALL), and management of stroke in sickle cell disease.

UPMC Children's Hospital of Pittsburgh is affiliated with the University of Pittsburgh School of Medicine and nationally ranked in nine clinical specialties by *U.S. News & World Report*.



About UPMC Children's Hospital of Pittsburgh

Regionally, nationally, and globally, UPMC Children's Hospital of Pittsburgh is a leader in the treatment of childhood conditions and diseases, a pioneer in the development of new and improved therapies, and a top educator of the next generation of pediatricians and pediatric subspecialists. With generous community support, UPMC Children's Hospital has fulfilled this mission since its founding in 1890. UPMC Children's is recognized consistently for its clinical, research, educational, and advocacy-related accomplishments, including ranking 13th among children's hospitals and schools of medicine in funding for pediatric research provided by the National Institutes of Health (FY2017).