Pediatric Insights

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT CANCER 2018-19

Fall 2018

An Update From the Division of Pediatric Hematology/Oncology

In This Issue

- New Director of Neuro-Oncology Program
- New Faculty Profile: Frederico Xavier, MD, MS
- About the Divisions
- Recent Publications
- A Novel Pilot Study of Telemedicine in Pediatric Cancer Survivor Transitions
- New Grant to Study Graft-Versus-Host Disease
- UPMC Physician Resources

Division Welcomes New Director of Neuro-Oncology Program

Alberto Broniscer, MD, MS, joined the UPMC Children's Hospital of Pittsburgh Division of Pediatric Hematology/Oncology in August 2017. Formerly with St. Jude Children's Research Hospital and The University of Tennessee Health Science Center (2002-2017), Dr. Broniscer has assumed the role of director of pediatric neuro-oncology at UPMC Children's. He brings with him more than two decades of clinical and research experience, with expertise in conducting clinical trials and studying multiple aspects of brain and spinal cord tumors in children, including diffuse intrinsic pontine glioma (DIPG).

A native of Brazil, Dr. Broniscer completed his medical degree and residency at the São Paulo University Medical School followed by fellowships at St. Jude Children's Research Hospital, the New York University School of Medicine, and Johns Hopkins University School of Medicine.

As the new director of the nationally recognized neuro-oncology program at UPMC Children's, Dr. Broniscer will be adding his tremendous talents and leadership to an already robust multi-disciplinary clinical apparatus and a research program engaged in a diverse portfolio of clinical, translational, and basic science investigations.

"There are two key aspects of my work as director of the neuro-oncology program. First is the daily care of patients with brain and spinal cord tumors, to bring excellence of care to these individuals, collaborating to provide the most advanced treatment protocols possible in coordination with our colleagues in pediatric neurosurgery, radiation oncology, pathology, behavioral medicine, ophthalmology, and all the other members of the team," says Dr. Broniscer.

The second aspect of Dr. Broniscer's work central to his role as program director is a continuing focus on research to better understand the basic biology of brain and spinal cord tumors, and to develop new treatments that may lead to improved standards of care for these rare cancers. "With many of these rare diseases, we are lacking, as a field, standard treatments and paradigms for care. This is largely due to the rarity of the conditions, and our incomplete basic biological understanding for how and why these cancers arise in our pediatric patients."

Continued on Page 7

UPMC CHILDREN'S HOSPITAL OF PITTSBURGH

New Faculty Profile: Frederico Xavier, MD, MS

Frederico Xavier, MD, MS, joined the UPMC Children's Hospital of Pittsburgh Division of Pediatric Hematology/Oncology as assistant professor of pediatrics in July 2017. He is also an associate director at the Hemophilia Center of Western Pennsylvania.

Dr. Xavier completed both his medical school and pediatric residency at the University of Campinas, São Paulo, Brazil, in 1997 and 2001, respectively. Dr. Xavier then completed a fellowship in pediatric hematology/oncology at the Federal University of São Paulo, Brazil, followed by a pediatric residency at Long Island College Hospital in Brooklyn, New York, and at the Schneider Children's Hospital, Long Island Jewish North Shore Program in Hyde Park, New York.

Dr. Xavier performed his pediatric hematology/oncology fellowship at both the St. Jude Children's Hospital, Memphis, Tennessee, and the Hospital for Sick Children, Toronto, Ontario, Canada, in 2011. His Master's degree in clinical research was obtained from the Indiana Hospital in Purdue University in 2014. Prior to his arrival at UPMC Children's Hospital, he held appointments as assistant professor of pediatrics and director of thrombosis and hemostasis at the Penn State Hershey Children's Hospital.

We have an expanding program at UPMC Children's with much investment devoted to becoming a national and international leader in pediatric hemostasis.

As a member of the growing Pediatric Hemophilia and Hemostasis and Thrombosis Programs at UPMC Children's, Dr. Xavier's clinical work focuses on the diagnosis and treatment of acquired and congenital bleeding and clotting disorders in children. "We have an expanding program at UPMC Children's with much investment devoted to becoming a national and international leader in pediatric hemostasis. This is one of the things that attracted me to join the program, along with the caliber of scientists and clinicians already here — Cheryl Hillery, Jake Cooper, Margaret Ragni, and the rest of the faculty are world-class researchers focused on expanding both our clinical care and basic science programs," says Dr. Xavier.

One of Dr. Xavier's clinical interests is in joint health in patients with hemophilia, and he is actively working on developing new protocols in terms of imaging, collaborating with colleagues in the Department of Radiology on MRI protocols. He also is undertaking training in ultrasound for use in surveillance of injured or surgically repaired joints in children who have hemophilia.

Transitionary care for children with hemophilia and other bleeding or clotting disorders as they age is of critical importance. Comprehensive care requirements for these conditions extend to everything from primary care to surgical care, even dental care. Patients must understand the various aspects of their disease and adapt to these changes over time, as they age, and become more responsible for their own health care needs and goals. "Our aim is to provide the most comprehensive care possible. This approach extends to patient education and the transitionary care process to ensure patients and their primary care providers are supported by our multidisciplinary teams who are experts in managing the complex and varied needs of bleeding and clotting disorders," says Dr. Xavier.

As associate director of the Hemophilia Center of Western Pennsylvania, a state and federally funded program that provides treatment, support, and clinical trials participation for both patients and families of adults and children with hemophilia and other bleeding and clotting conditions, Dr. Xavier is responsible for patient care and various aspects of research and ongoing clinical trials.

With respect to research, Dr. Xavier and the Hemostasis and Thrombosis Program are currently involved in several clinical trials, including Kids-DOTT, a randomized international prospective study assessing the safety of a short duration anticoagulation course in provoked pediatric thrombosis and an observational industry-based study using non-factor medications in patients with hemophilia. "It is a groundbreaking time in pediatric hemostasis and UPMC Children's is part of it," says Dr. Xavier.

Continued on Page 4

About the 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 and the University of Pittsburgh Cancer Institute.

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

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

About the 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.

New Faculty Profile *Continued from Page 2*

The UPMC Children's program also is part of a national taskforce working to identify risk factors for the development of thrombosis in children and create a prevention protocol that can be used to guide physicians. "If, as an adult, you are admitted for a knee replacement or other surgery, guidelines are in place to mitigate clot formation. For pediatric patients, we have yet to develop a standard protocol, so this taskforce is actively working to develop these guidelines." Several other initiatives Dr. Xavier has joined since his arrival include participation in the Pharmacy Department Anticoagulation Committee, and the ECMO team's Anticoagulation Taskforce. Within the Division of Pediatric Hematology/Oncology, Dr. Xavier and counterparts, through the Coagulation Committee, have undertaken the process of reviewing educational materials distributed for both inpatient and outpatient settings as part of a broader initiative at UPMC Children's related to patient education materials.

References and Further Reading

For further information about Dr. Xavier's past research, please see the following published papers.

1. Xavier F, Komvilaisak P, Williams S, Kulkami AV, deVeber G, Moharir MD. Anticoagulant Therapy in Head Injury-associated Cerebral Sinovenous Thrombosis in Children. *Pediatr Blood Cancer.* 2014; 61(11): 2037-2042.
2. Chan MW, Leckie A, Xavier F, Uleryk E, Tadros S, Blanchette V, Doria AS. A Systematic Review of MR Imaging as a Tool for Evaluating Haemophilic Arthropathy in Children. *Haemophilia.* 2013; 19(6): 324-334.
3. Sultan S, et al; IPSS Investigators. Dyslipidemia in Children With Arterial Ischemic Stroke: Prevalence and Risk Factors. *Pediatr Neurol.* 2018; 78: 46-54.

Recent Publications

Klei LR, et al. MALT1 Protease Activation Triggers Acute Disruption of Endothelial Barrier Integrity via CYLD Cleavage. *Cell Rep.* 2016; 17(1): 221-232.

Rosebeck S, Lim MS, Elenitoba-Johnson KS, McAllister-Lucas LM, Lucas PC. API2-MALT1 Oncoprotein Promotes Lymphomagenesis Via Unique Program of Substrate Ubiquitination and Proteolysis. *World J Biol Chem.* 2016; 7(1): 128-37.

Zappia KJ, Guo Y, Retherford D, Wandersee NJ, Stucky CL, Hillery CA. Characterization of a Mouse Model of Sickle Cell Trait: Parallels to Human Trait and a Novel Finding of Cutaneous Sensitization. *Br J Haematol.* 2017; 179(4): 657-666.

Carden MA, Smith S, Meany H, Yin H, Alazraki A, Rapkin LB. Platinum Plus Bortezomib for the Treatment of Pediatric Renal Medullary Carcinoma: Two Cases. *Pediatr Blood Cancer.* 2017; 64(7). Epub 2017 Jan 4.

Bailey KM, Airik M, Krook MA, Pedersen EA, Lawlor ER. Micro-Environmental Stress Induces Src-Dependent Activation of Invadopodia and Cell Migration in Ewing Sarcoma. *Neoplasia.* 2016; 18(8): 480-8.

Bukowinski AJ, Burns KC, Parsons K, Perentesis JP, O'Brien MM. Toxicity of Cancer Therapy in Adolescents and Young Adults (AYAs). *Semin Oncol Nurs.* 2015; 31(3): 216-26.

Cooper JD, Ritchey AK. Response to Treatment and Adverse Events Associated With Use of Recombinant Activated Factor VII in Children: A Retrospective Cohort Study. *Ther Adv Drug Saf.* 2017; 8(2): 51-59.

Cooper JD, Costello AG, Shaw PH. A Comparison of Extremity Thrombosis Rates in Adolescent and Young Adult Versus Younger Pediatric Oncology Patients at a Children's Hospital. *J Adolesc Young Adult Oncol.* 2017; 6(1): 62-66.

Owusu-Ansah A, Ihunnah CA, Walker AL, Ofori-Acquah SF. Inflammatory Targets of Therapy in Sickle Cell Disease. *Transl Res.* 2016; 167(1): 281-97.

O'Halloran K, Ritchey AK, Djokic M, Friehling E. Transient Juvenile Myelomonocytic Leukemia in the Setting of PTPN11 Mutation and Noonan Syndrome With Secondary Development of Monosomy 7. *Pediatr Blood Cancer.* 2017; 64(7). Epub 2017 Jan 13.

Kelly JA, May CS, Maurer SH2. Assessment of the Spiritual Needs of Primary Caregivers of Children with Life-Limiting Illnesses Is Valuable Yet Inconsistently Performed in the Hospital. *J Palliat Med.* 2016; 19(7): 763-6.

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

Jackson LE, et al. Genetic Dissociation of Glycolysis and the TCA Cycle Affects Neither Normal nor Neoplastic Proliferation. *Cancer Res.* 2017; 77(21): 5795-5807.

Proud L, Ritchey AK. Management of Type 2b von Willebrand Disease in the Neonatal Period. *Pediatr Blood Cancer.* 2017; 64(1): 103-105.

Seynnaeve B, Lee S, Borah S, Park Y, Pappo A, Kirkwood JM, Bahrami A. Genetic and Epigenetic Alterations of TERT Are Associated with Inferior Outcome in Adolescent and Young Adult Patients with Melanoma. *Sci Rep.* 2017 Apr 5;7:45704. Epub ahead of print.

Costello AG, Nugent BD, Conover N, Moore A, Dempsey K, Tersak JM. Shared Care of Childhood Cancer Survivors: A Telemedicine Feasibility Study. *J Adolesc Young Adult Oncol.* 2017; 6(4): 535-541.

Nugent BD, Moore A, Costello A, Lewarchik AM, Tersak JM. Partnering to Optimize Care of Childhood Cancer Curvivors. *J Fam Pract.* 2017 Apr; 66(4):E1-E6.

Makadia P, et al. Aplastic Anemia and Cytotoxic T Lymphocyte Antigen-4 Haploinsufficiency Treated With Bone Marrow Transplantation. *J Allergy Clin Immunol Pract.* 2017;5(5): 1445-1447. Epub 2017 May 9.

A Novel Pilot Study of Telemedicine in Pediatric Cancer Survivor Transitions

A group of researchers from the Division of Pediatric Hematology/Oncology at UPMC Children's Hospital of Pittsburgh published findings from a new telemedicine pilot study examining the benefits of the technology in transitioning survivors from the oncology clinic to the primary care clinic. **Jean M. Tersak, MD**, director of the Survivorship Program and principal investigator of the Children's Oncology Group, and colleagues from the Division and the University of Pittsburgh School of Nursing published their findings in December 2017 in the *Journal of Adolescent and Young Adult Oncology.*

Their pilot study points out that with the growing number of pediatric cancer patients surviving into adulthood, there is a need to develop better models of transition of care from the pediatric oncologist to the adult primary care provider. Dr. Tersak's group sought to understand from a group of primary care providers and childhood cancer survivors their assessment of the use of the telemedicine technology during a regular office visit while discussing aspects of transition with a member of Pediatric Survivorship Clinic. A structured post-visit questionnaire was given to individuals from 19 transition visits. Survey results indicate that both the primary care providers and the survivors felt better versed and more comfortable in the care. This pilot study will provide a foundation for further research in the area by Dr. Tersak and her colleagues in the Survivorship Clinic.

The transition process is complex and highly individualized. Long-term childhood cancer survivors have needs that go beyond their basic primary care. Late effects of cancer treatments are a potential for many survivors and may appear months to even years after completion of therapy. Geographical barriers between where individuals may have received their oncology care versus where they are receiving their primary care as survivors can be challenging. The use of telemedicine consults to overcome this barrier has the ability to facilitate ongoing communications during the transition process that would otherwise be difficult or time consuming. As their paper concludes, more research is needed to standardize what these telemedicine consults should consist of, and how they can be evaluated to provide meaningful feedback for further refinement and improvement of the telemedicine process.

To learn more about the Survivorship Clinic at UPMC Children's, its clinical programs, resources, and ongoing research projects, please visit **CHP.edu/Cancer**.

References and Further Reading

1. Costello AG, Nugent BD, Conover N, Moore A, Dempsey K, Tersak JM. Shared Care of Childhood Cancer Survivors: A Telemedicine Feasibility Study. *J Adolesc Young Adult Oncol.* 2017 Dec; 6(4): 535-541. Epub ahead of print.
2. Nugent BD, Moore A, Costello A, Lewarchik AM, Tersak JM. Partnering to Optimize Care of Childhood Cancer Surviors. *J Fam Pract.* 2017; 66(4): E1-E6. Review.
3. 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.

Pediatric Cancer Survivorship Clinic Staff

Jean M. Tersak, MD
Director, Survivorship Clinic

Bethany Nugent, PhD, RN
Nurse Researcher

Rachel Young, MSN, CRNP, AOD
Nurse Practitioner

Aimee Costello, RN, MSN, CRNP
Coordinator, Survivorship Clinic

Noelle Conover, MS
Project Coordinator, SurvivorConnect

Eileen Weinmann, RN, CPN
RN Coordinator

New Grant to Study Graft-Versus-Host Disease

Craig A. Byersdorfer, MD, PhD, is a pediatric hematologist/oncologist in the Division of Blood and Marrow Transplantation and Cellular Therapies, with a research focus on understanding posttransplant complications, specifically graft-versus-host disease (GVHD) and the role that T cells play in driving this condition.

"Graft-versus-host disease affects 30 to 50 percent of transplant patients and has been an intractable problem for decades. We even know that GVHD is a T-cell driven phenomenon. If we can modulate T-cell metabolism in a way that shuts down the most active cells driving the condition, or identify metabolic ways to eliminate them altogether, we will make blood and marrow transplantation (BMT) a safer and more effective therapy for individuals with otherwise incurable diseases," says Dr. Byersdorfer.

In February, Dr. Byersdorfer received one of four Amy Strelzer Manasevit Research Program grants awarded by the Be The Match Foundation® in 2018. Handed out for either clinical or preclinical investigation of complications arising after allogeneic hematopoietic stem cell transplantation (alloHSCT), the award is administered over three years with a maximum support of $240,000.

A central focus of Dr. Byersdorfer's research is how T cell metabolism and the targeting of metabolic pathways, may be used to help limit, or even eliminate, GVHD post-transplant. Previous research by Dr. Byersdorfer and his team has demonstrated that the cellular energy sensor, AMP-activated protein kinase (AMPK), plays a necessary role in T cells in GVHD models, and his belief is that modulating this pathway may result in a decreased incidence of GVHD following allogeneic transplantation in humans.

Dr. Byersdorfer's new award will be used to investigate the mechanism of AMPK's action in post-transplant T cells and determine the relationship by which AMPK is linked to pro-inflammatory cytokines like IL-6. "We seek to further clarify the relationship between AMPK, metabolic stress, and cytokine sensitivity, and to translate these findings into human T cells. If successful, these new studies will help to define novel mechanisms downstream of metabolic reprogramming in activated T cells, that may facilitate development of innovative treatments for GVHD, while at the same time maintaining homeostatic immunity and anti-leukemia responses following alloHSCT," says Dr. Byersdorfer.

UPMC Physician Resources:

CME, News, Events for Physicians from UPMC

Publications, free continuing medical education, and other resources are available by visiting **UPMCPhysicianResources.com/Pediatrics.** 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.

New Director of Neuro-Oncology Program *Continued from Page 1*

Current Research Highlights

Since arriving at UPMC Children's in August, Dr. Broniscer has become involved in several clinical trials using immunotherapy (vaccines) for low-grade gliomas and recurrent ependymomas[4-6], all of which are ongoing with patient recruitment.

As a current member of the Pediatric Brain Tumor Consortium, Dr. Broniscer has been involved in many past investigations and is currently leading one national clinical trial studying immune checkpoint inhibitors in patients whose brain tumors contain large numbers of genetic abnormalities. "These are rare, deadly tumors that we are hopeful will show improved response to this recently FDA-approved agent being used in adult patients whose tumors have an excessive number of genetic abnormalities," says Dr. Broniscer.

DIPG and Plans for New Research

A significant portion of Dr. Broniscer's past work has been related to the devastating diffuse intrinsic pontine glioma. Most likely the deadliest of all pediatric brain cancers, this aggressive brain stem malignancy remains incurable and difficult to treat due to its invasive nature in the pons and surrounding structures, which are areas that contain crucial basic life support functions. Current standards of care have changed little in the last three decades with radiotherapy being the accepted route to achieve temporary symptom reduction and a slowing of disease progression.

Progress has been made on several fronts in recent years, notably in the ability to safely biopsy these tumors, when warranted, which has allowed for an increase in tissue samples available to be analyzed. Routine biopsies are still typically not done for many reasons, although clinicians and researchers in France and some locations in the United States have begun to do this regularly in recent years. "These biopsies can be done safely, and I think in the future, we'll be doing more of them, more frequently. As it stands right now, we simply do not have the tools to choose the best possible treatments based on the genetic findings from the tumor obtained at biopsy.[7] This will change, I hope, soon, and then the benefits of biopsy will really become relevant as physicians may be able to adjust treatment based on actionable genetic findings in each tumor," says Dr. Broniscer.

Past work by Dr. Broniscer and colleagues has revealed, in a study published in 2008, a different disease trajectory in individuals diagnosed with DIPG at a younger age. "In these individuals, we found that the biology of the tumors was markedly different than in cases of later onset. Younger patients with DIPG responded more favorably to the standard treatment; however, the end outcome is still fatal with this disease. This clinical observation was later validated by showing that DIPG in younger patients harbors different genetic abnormalities than tumors from older children," says Dr. Broniscer.

Since his arrival, Dr. Broniscer has been working to design new research and clinical trials. "We are working to develop new studies of the biology of brain and spinal cord tumors in children, and to potentially design clinical trials for affected patients. To be here at UPMC Children's, leading the neuro-oncology group and collaborating with so many of our other world-class departments and people, it's an exciting time to be working in this field, and I'm privileged to help lead the way forward."

References and Further Reading

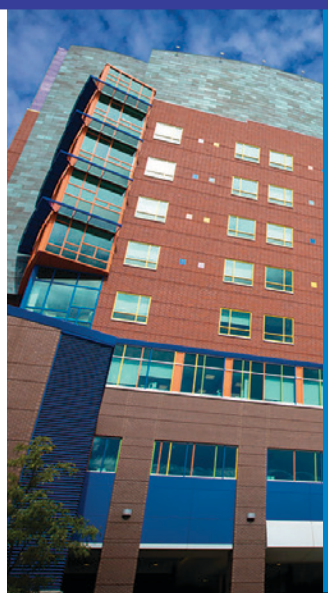
A sample of Dr. Broniscer's most recent publications and his current open clinical trials are below.

1. 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 Feb 10. doi: 10.1007/s00401-018-1814-2. Epub ahead of print.
2. Patay Z, Merchant TE, Nguyen R, Pierson CR, Onar-Thomas A, Broniscer A.Treatment-Related Noncontiguous Radiologic Changes in Children With Diffuse Intrinsic Pontine Glioma Treated With Expanded Irradiation Fields and Antiangiogenic Therapy. *Int J Radiat Oncol Biol Phys.* 2017 Dec 1; 99(5): 1295-1305. doi: 10.1016/j.ijrobp.2017.08.021. Epub 2017 Aug 24.
3. Kilburn LB, Kocak M, Baxter P, Poussaint TY, Paulino AC, McIntyre C, Lemenuel-Diot A, Lopez-Diaz C, Kun L, Chintagumpala M, Su JM, Broniscer A, Baker JN, Hwang EI, Fouladi M, Boyett JM, Blaney SM. A Pediatric Brain Tumor Consortium Phase II Trial of Capecitabine Rapidly Disintegrating Tablets With Concomitant Radiation Therapy in Children With Newly Diagnosed Diffuse Intrinsic Pontine Gliomas. *Pediatr Blood Cancer.* 2018 Feb; 65(2). doi: 10.1002/pbc.26832. Epub 2017 Nov 1.
4. Immunotherapy for Recurrent Ependymomas in Children Treatment for Recurrent Ependymomas Using HLA-A2 Restricted Tumor Antigen Peptides in Combination With Imiquimod. ClinicalTrials.gov Identifier: NCT01795313.
5. A Pilot Study of Glioma Associated Antigen Vaccines in Conjunction With Poly-ICLC in Pediatric Gliomas. ClinicalTrials.gov Identifier: NCT01130077.
6. A Vaccine Trial for Low Grade Gliomas. ClinicalTrials.gov Identifier: NCT02358187.
7. Biological Medicine for Diffuse Intrinsic Pontine Glioma (DIPG) Eradication (BIOMEDE). ClinicalTrials.gov Identifier: NCT02233049.

UPMC | CHILDREN'S HOSPITAL OF PITTSBURGH

4401 Penn Ave.
Pittsburgh, PA 15224

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).

USNW507158 AS/MP 9/18