Children's Mercy KANSAS CITY

HEMATOLOGY, ONCOLOGY AND BLOOD AND MARROW TRANSPLANTATION

A MESSAGE FROM Alan Gamis, MD, MPH

Interim Division Director, Hematology/Oncology/BMT
Associate Division Director, Section of Oncology

In the Division of Pediatric Hematology, Oncology and Blood and Marrow Transplantation at Children's Mercy Kansas City, the families who enter our doors receive cutting-edge clinical care for nearly every type of childhood cancer, as well as sickle cell disease, hemophilia and other blood disorders.

For nearly 40 years, we have been an integral part of research trials through our continuous participation as the region's only NCI Children's Oncology Group (COG) cancer center. Discoveries from our trials have also led to the early introduction into standard care for the children who followed and benefited from their predecessors' pay-it-forward mindset.

Today, Children's Mercy has expanded our research footprint to become a center of discovery through the Children's Mercy Research Institute. The institute is home to our highly recognized Cancer Genomics center, rapidly growing Cancer Immunotherapeutics program, expanding Survive & Thrive program and Cancer Biology labs, along with a multitude of other state-of-the-art research programs. Joint research and clinical programs with our partner institutions are ever expanding to provide many new benefits to our patients.

But research must also have a partner — the complete and compassionate delivery of top-notch care. It takes a village, a team, to fully envelop our children and their families in the care that helps them deal with the devastating diagnosis of cancer and disease and emerge as thriving survivors on the other side of this journey. We are blessed at Children's Mercy to have the best of these two worlds, research and compassionate care, from which we may confidently say our children need not go anywhere else.

2021 HIGHLIGHTS

There has been a greater than **50% increase** over the previous year in patients being enrolled in **Children's Oncology Group therapeutic studies**. In addition, **nearly 100 patients** diagnosed with cancer have consented to have specimens collected for research purposes.

The Hemophilia Treatment Center (HTC) cares for **more than 800 patients** with bleeding disorders annually.

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT CANCER 2021-22

Once again ranked in the **top 30 pediatric oncology programs (#28)** in the nation, according to U.S. News & World Report.

Children's Mercy is a consortium partner of the **NCI-designated** University of Kansas Cancer Center.

The sickle cell disease team cares for **more than 300 patients** each year.

Accredited by the Foundation for the Accreditation of Cellular Therapy.

FY 2021 By the Numbers

Comprehensive Clinical Care

Children's Mercy offers a breadth and depth of expertise in Hematology/Oncology/BMT with 24 faculty.

Hematology

The sickle cell program offers comprehensive care and includes specialty services, such as a Sickle Cell Pulmonology Clinic and Sickle Cell Integrative Persistent Pain Clinic. The Hemophilia Treatment Center (HTC) is a federally-designated treatment center that provides the latest, most advanced treatments for patients with bleeding disorders. Children's Mercy also offers one of the only pediatric stroke centers in the country, bringing together specialists from hematology/oncology, neurology and rehabilitative medicine. Children's Mercy also has a dedicated inpatient coagulation consult service.

Hematology	
Sickle Cell	
Active Sickle Cell Patients	290
Active Pediatric Bleeding Disorder Patients by Type	
F9 Deficiency	56
F8 Deficiency	198
vWD	264
Plt Dysfunction	78
FI, V, VII, X, XII Deficiencies	58
Other Hematology Disorders	100*
Total	1,044

*Estimate

BMT and Cellular Therapy

The BMT team offers advanced treatment for leukemia, brain tumors, Hodgkin and non-Hodgkin lymphoma and a range of other cancer diagnoses. The innovative program has expanded its scope, with successful transplants that address a variety of rare and nonmalignant diseases. The team has experience performing haploidentical transplants, is at the forefront of cellular therapy for children, and is an experienced provider of Kymriah treatment for qualifying patients.

Blood and Marrow Transplantation	
Disease	# of Transplants
Acute Lymphoblastic Leukemia	1
Acute Myeloid Leukemia	6
Acute Lymphoblastic Leukemia/ Acute Myeloid Leukemia	2
Atypical Teratoid Rhabdoid Tumor	3
Beta Thalassemia	1
Hodgkin Lymphoma	1
Juvenile idiopathic arthritis	1
Medulloblastoma	7
Metabolic Diseases	2
Myelodysplastic syndrome/AML	1
Myelodysplastic syndrome/ Shwachman-Diamond	1
Neuroepithelial tumor	2
Pineoblastoma	3
Retinoblastoma	1
Severe Aplastic Anemia	6
Total	38

Cellular Therapies	
Disease	# of Infusions
Acute Lymphoblastic Leukemia	9
Acute Myeloid Leukemia	1
Total	10
HCT	# of Infusions
Allogeneic	21
Autologous	17
Total	38
Cellular Therapy	# of Infusions
Allogeneic	1
Autologous	9
Total	10

Joel Thompson, MD, and patient

Oncology

Children's Mercy is a consortium partner of the National Cancer Institute-designated University of Kansas Cancer Center. The relationship creates increased resources for our researchers and brings cutting-edge cancer therapy to young patients. The specialists offer care for a range of conditions, as well as specialized programs that cross multiple service lines and support various patient populations.

Five-Year Pediatric Cancer Survival Percentage*		
Type of Cancer	# Patients	Overall Five-Year Survival Rate
Acute Lymphoblastic Leukemia	342	92.9%
Acute Myeloid Leukemia	80	48.10%
Neuroblastoma	100	85.81%
Rhabdomyosarcoma	54	66.72%
Wilms Tumor	61	96.52%

*Patients diagnosed 2009-2019

CLINICAL EXCELLENCE SETTING NEW STANDARDS OF CARE

Sickle Cell and Pulmonary Clinic

Initially created as a quarterly clinic a decade ago, the Sickle Cell and Pulmonary Clinic at Children's Mercy now operates monthly, providing comprehensive care to 40 pediatric patients. Children with sickle cell disease also receive treatment for recurring related pulmonary issues such as asthma, allergies, sleep apnea and acute chest syndrome. The lead pediatric pulmonologist, Alvin Singh, MD, works alongside the comprehensive sickle cell team members, M. Laurence Noisette, MD; Julie Routhieaux, RN, APRN; Susie Sarcone-Jones, RN, APRN; and Areli Ramphal, LMSW, Sickle Cell Social Worker. A respiratory therapist is always available for pulmonary function testing and education, such as reviewing asthma action plans. The clinic benefits patients and their families, not only because of the convenience of the combined care visit but also the seamless teamwork occurring between our health care professionals.

Cancer Genomics

The Children's Mercy Cancer Genomics Program brings together pediatric oncologists, molecular pathologists, genomics research faculty, bioinformaticians, genetic counselors, and many more, with the primary goal to improve survival through genomics sequencing. We offer comprehensive somatic and germline molecular testing to every child treated for cancer at Children's Mercy. In cases where we identify a genetic variant that predisposes to cancer, we offer genetic counseling and testing to immediate family members. Additionally, our team is actively leading genomics research projects in leukemia, lymphoma, solid tumors and brain tumors. We are exploring the underlying biology driving childhood cancers and, through collaborative partnerships with the University of Kansas Cancer Center, the National Cancer Institute, and other pediatric hospitals, we are committed to sharing our knowledge and accelerating the pace of genomics discoveries.

Global Health Work

The Children's Mercy HOPE Clinic and Research Program is committed to addressing global disparities in childhood cancer. Much of our work is centered in Mexico, where pediatric cancer is the leading cause of death in children, and approximately 90% of patients present with advanced-stage disease. Our team is conducting three open studies investigating the genetic differences among Mexican children with leukemia and sarcomas. However, our mission far exceeds research. We also educate oncology nursing teams and provide seminars on early detection for primary care physicians. We have been instrumental in producing educational videos in seven indigenous languages in Mexico, explaining the most common presenting signs and symptoms of cancer to help facilitate a prompt referral to a pediatric oncologist. Through this important work, we envision the creation of hope without borders for all children battling cancer.

Terrie Flatt, DO, MA, and Elaina

ACUTE LYMPHOBLASTIC LEUKEMIA: ELAINA'S STORY

It was just a typical busy morning for the Guerra family when the doctor called with their daughter's bloodwork results, saying the unexpected words that changed their world forever: "We think it's leukemia."

Like many Hispanic children, 4-year-old Elaina was at higher risk for certain types of aggressive childhood leukemia and other cancers, and concerningly, showed an inconsistent response to treatment. The medical community still struggles to fully understand how genetics plays a role in cancer, and participants from the Hispanic community are significantly underrepresented in clinical trials. While the majority of white children with standard-risk leukemia will likely be cured, the rate for Hispanic children is much lower.

Elaina and her family packed their bags and went straight to the Children's Mercy HOPE Clinic to meet with Terrie Flatt, DO, MA, a pediatric hematologist/oncologist who is fluent and medically trained in Spanish. The HOPE Clinic provides bilingual clinical services for Spanish-speaking families and a strong network of support as they navigate treatment. At HOPE, promising new targeted therapies, such as CAR T-cell therapy and other immunotherapies, are helping kids with difficult-to-treat cancers have a better shot at a cancer-free life.

Families also benefit from the innovative research done by Dr. Flatt, who along with collaborating institutions in Mexico, is conducting studies to investigate genetic links between ethnicity and how patients respond to treatment. The Children's Mercy Cancer Center Genomics Program is becoming a leader in pediatric translational research and is at the forefront of breakthroughs in treating, diagnosing and preventing complex childhood diseases.

Today, Elaina is in remission and is back to being herself. But her mother still holds her breath every time she receives Elaina's test results. For her family, the pediatric cancer research and treatment happening at Children's Mercy is deeply personal and life changing.

LEADING THE WAY Through Research

We continue to focus on researching new and better treatments for our patients within the division. By building collaborations within and outside of our institution, we have been able to build our footprint to include partnerships with, among others, Hospital for Sick Kids, Children's Hospital of Philadelphia, Children's of Orange County, Children's of Los Angeles, Stanford and Indiana University. Our local partnerships with KU and Stowers and our continued participation in multiple consortia also remain strong.

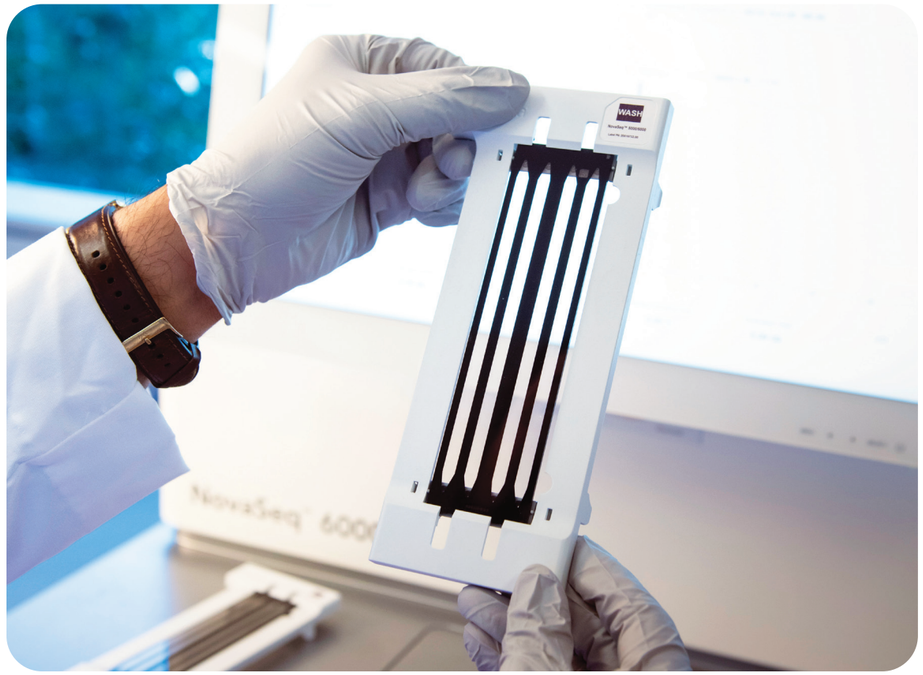
With the opening of the Children's Mercy Research Institute, opportunities to partner with bench scientists to move work to the bedside are becoming a reality. Awarded grants from the Masonic Cancer Alliance are helping our physicians and laboratory experts create the pathways for new treatments for sarcomas and leukemias.

By the Numbers

42 published manuscripts and book chapters

Participation in clinical trials

- Registry and Repository IRB approvals: **20** studies with **457** subjects
- Clinical studies: **68** enrolling studies with **84** enrolled in FY 2021



RESEARCH HIGHLIGHTS

Hall EM, Yin DE, Goyal RK, et al. Tisagenlecleucel infusion in patients with relapsed/refractory ALL and concurrent serious infection [published correction appears in *J Immunother Cancer*. 2021 Oct;9(10):]. *J Immunother Cancer*. 2021;9(1):e001225. doi:10.1136/jitc-2020-001225

In this two-patient case study conducted by Erin M. Hall, MD, Dwight E. Yin, MD, Rakesh K. Goyal, MD, et al., Tisagenlecleucel, an anti-CD19 chimeric antigen receptor T (CAR-T) cell therapy allowed the patients — a preschool-aged Hispanic female and a 23-year-old male — to achieve remission in otherwise refractory pediatric/young adult B-cell acute lymphoblastic leukemia (B-ALL). Publication of these case studies and others may guide providers and families as they face similarly challenging circumstances. While these cases represent successful infection management during CAR-T cell therapy, they should not be viewed as typical or even likely outcomes. Instead, they highlight the importance of clear communication with families, and the need for treatment carried out in a setting with extensive institutional knowledge by an experienced team with the ability to customize standard protocols.

Jaffray J, Branchford B, Goldenberg N, et al. Development of a risk model for pediatric hospital-acquired thrombosis: A report from the Children's Hospital-Acquired Thrombosis Consortium. *J Pediatr.* 2021;228:252-259.e1. doi:10.1016/j.jpeds.2020.09.016

According to the National Blood Clot Alliance, as many as 1 in 200 children will develop a blood clot while hospitalized. In a study published in the January 2021 issue of the *Journal of Pediatrics*, Michael S. Silvey, DO, et al., designed an assessment model to evaluate the risk of thrombosis in pediatric patients. This was done as part of the Children's Hospital-Acquired Thrombosis Registry, a multi-institutional registry for participants aged 0-21 years. Factors included age, cancer, congenital heart disease, other high-risk conditions (such as inflammatory/autoimmune disease, blood-related disorder, protein-losing state, total parenteral nutrition dependence, thrombophilia/personal history of VTE), recent hospitalization and immobility. Once the greatest-risk groups have been identified and validated, future clinical trials will study prevention and treatment strategies.

Pollard JA, Guest E, Alonzo TA, Gerbing RB, Loken MR, Brodersen LE, Kolb EA, Aplenc R, Meshinchi S, Raimondi SC, Hirsch B, Gamis AS. Gemtuzumab ozogamicin improves event-free survival and reduces relapse in pediatric KMT2A-rearranged AML: Results from the phase III Children's Oncology Group trial AAML0531. *J Clin Oncol*. 2021 Oct 01; 39(28):3149-3160. PMID: 34048275

From this phase III clinical trial that provided data to support the approval of gemtuzumab ozogamicin (GO) in children, Erin M. Guest, MD, and Alan S. Gamis, MD, MPH, et al., studied whether GO, in combination with conventional chemotherapy, provided therapeutic benefit for pediatric patients with KMT2A-rearranged (KMT2A-r) acute myeloid leukemia (AML). The trial enrolled 1,022 patients, 21% of whom had KMT2A-r AML. Results showed GO significantly improved event-free survival and reduced relapse risk, both in overall and in higher- and lower-risk KMT2A-r patients. Even patients with lower CD33 expression benefited from GO. An improved 5-year disease-free survival rate of 57% was reported among patients in the GO group compared with 33% of patients in the non-GO group. Consolidated therapy with hematopoietic stem cell transplant may provide additional clinical benefit, however, this needs to be studied further.

Ehrhardt MJ, Ward ZJ, Liu Q, et al. Cost-effectiveness of the International Late Effects of Childhood Cancer Guideline Harmonization Group screening guidelines to prevent heart failure in survivors of childhood cancer. *J Clin Oncol*. 2020;38(33):3851-3862. doi:10.1200/JCO.20.00418

Joy M. Fulbright, MD, et al., participated in a study investigating the need and frequency of screening echocardiograms for survivors of childhood cancer who are at an increased risk for heart failure. Following the development of a simulation model, the authors evaluated the long-term health outcomes for high, moderate and low-risk survivors — weighed against the economic impact of this procedure. While current international guidelines recommend screening every five years for all risk groups, the findings suggest that screening for low-risk survivors could potentially be reduced or discontinued, and that clinicians should increase screening to once every two years for high-risk survivors. In general, routine screening reduced the risk by 4% to 11%, depending on frequency.

M Weerakoon-Ratnayake K, Vaidyanathan S, Larky N, et al. Microfluidic device for on-chip immunophenotyping and cytogenetic analysis of rare biological cells. *Cells*. 2020;9(2):519. Published 2020 Feb 24. doi:10.3390/cells9020519

Keith August, MD, MS, and the Children's Mercy research team are collaborating with the lab of Steven Soper, PhD, at the University of Kansas to develop a chip technology that can detect Circulating Leukemia Cells in children with acute lymphoblastic leukemia. By using microfluidics, investigators are hoping to recognize early resistance to treatment and eliminate the need for bone marrow testing.

Myers GD, Verneris MR, Goy A, Maziarz RT. Perspectives on outpatient administration of CAR-T cell therapy in aggressive B-cell lymphoma and acute lymphoblastic leukemia. *J Immunother Cancer*. 2021;9(4):e002056. doi:10.1136/jitc-2020-002056

Although initially administered in the inpatient setting, there has been a growing interest in delivering CAR-T cell therapy as outpatient treatment. Doug Myers, MD, et al., presented institutional experience in the preparation and coordination of this outpatient therapy, which has not yet been adopted as standard clinical practice due to logistic and reimbursement issues.

Konkle BA, Quon DV, Raffini L, et al. A prospective observational study of antihemophilic factor (recombinant) prophylaxis related to physical activity levels in patients with hemophilia A in the United States (SPACE). *J Blood Med*. 2021;12:883-896. Published 2021 Oct 14. doi:10.2147/JBM.S327180

Shannon Carpenter, MD, MSCI, FAAP, et al., conducted a six-month study to explore the relationship between physical activity levels, FVIII infusion timing, and occurrence of bleeding in patients with severe/moderately severe hemophilia. Patients received an eDiary application and a wearable activity tracker, with results showing that activities with a high risk of collision lead to an increased risk of bleeding.

Genomic Answers for Kids Advances Rare Disease Research

The Children's Mercy Research Institute has released more than 2,300 pediatric rare disease genomes through its Genomic Answers for Kids (GA4K) program, which makes it one of the largest pediatric rare disease whole genomic datasets ever publicly shared.

To date, more than 3,700 patients have enrolled in the program, which has resulted in more than 18,000 new genomic analyses and more than 600 genetic diagnoses. In addition, the program has advanced research genomic analyses for children of 350 families with more common childhood diseases: cerebral palsy and Down syndrome.

The full pediatric data repository is shared in a real-time web interface through a comprehensive process, which gives researchers and clinicians low-barrier access to processed data with disease prioritized genetic changes.

"Giving access to our data allows researchers to link their own genetic findings so they can accept or reject hypotheses on their gene discoveries," said Tomi Pastinen, MD, PhD, Director, Genomic Medicine Center, Children's Mercy Kansas City. "Data sharing is the only way we'll make headway in the quicker delivery of results that are non-diagnostic today."

The GA4K program has helped hundreds of kids, like Celia, find a genetic diagnosis.

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Children's Mercy KANSAS CITY

THE UNIVERSITY OF KANSAS CANCER CENTER

NCI Cancer Center
A Cancer Center Designated by the National Cancer Institute

LEARN MORE ABOUT THE DIVISION OF HEMATOLOGY, ONCOLOGY AND BLOOD AND MARROW TRANSPLANTATION.

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