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### CANCER REGISTRY

### SARCOMAS
- Osteosarcoma
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### PATIENT FEATURE:
- Kambre Konrade
- Alexander Goodwin
- Persephone Consuela Duran

### DIAGNOSTIC AND TREATMENT SUPPORT SERVICES
- Pathology
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- Cytogenetics
- Advanced Practice Provider
- Experimental Therapeutics
- Cancer Predisposition Clinics and Genome Center
- FaCT

### RESEARCH
- Research Focuses on More Effective Sarcoma Therapy

### CHILDREN’S MERCY CANCER CENTER PROGRAMS

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This year’s Children’s Mercy Cancer Annual Report focuses on the most common sarcomas seen in children: osteosarcoma, Ewing sarcoma and rhabdomyosarcoma. Sarcomas are a diverse group of tumors that still remain a significant challenge in pediatric oncology.

Sarcomas occur in connective tissues, most commonly the bones, muscles, tendons or cartilage. While osteosarcoma occurs in the bones, rhabdomyosarcoma occurs in the soft tissues and muscles anywhere in the body, and Ewing sarcoma can occur in bone or soft tissues.

Curative therapy requires advanced pathologic and genetic techniques, as well as advanced radiologic scanning to determine the extent of disease and guide therapy. All of these tumors need aggressive chemotherapy, which can take up to a year to complete. During this time, our patients can suffer infections and side effects of chemotherapy, often requiring the multidisciplinary subspecialty care available at Children’s Mercy.

While chemotherapy is important, another crucial factor in the ability to cure sarcomas is “local control.” Local control refers to the ability to control the primary tumor, either by surgery or radiation. We work closely with our surgical colleagues, both at Children’s Mercy and at the University of Kansas Cancer Center, to provide the best surgical care and radiation oncology.

Once patients and their families make it through the long road of chemotherapy and local control, we enter a long waiting process to monitor for disease relapse and long-term side effects from chemotherapy. Patients usually need to continue in extensive physical therapy and rehabilitation, depending on the location of their tumor.

This year’s annual report illustrates the breadth and depth of clinical care, diagnostic capabilities, research and psychosocial supports we provide at Children’s Mercy. Today, a child with sarcoma has a much greater chance of cure than was possible 20 or 30 years ago, but we still have a long way to go to be able to cure every child.

This has been an exciting year for the Children’s Mercy Cancer Center as it adds to its National Cancer Institute activity with Children’s Oncology Group the new designation as an NCI-designated cancer center by virtue of its new consortium status with the University of Kansas Cancer Center. Research leading to current and future improvements in cancer care are a cornerstone of this designation. We present a small part of that research in this year’s annual report. As the new Children’s Research Institute embarks on the construction of its nine-story research building, this is just a small taste of what is to come in childhood cancer research here in Kansas City.

Thank you to our donors and volunteers whose philanthropic support sustains our work, and to the staff at Children’s Mercy who tirelessly works to support our patients and their families. And thank you most of all to the patients and their families who allow us to care for them and guide them through this difficult journey.

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Katherine M. Chastain, MD
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The Cancer Registry at Children’s Mercy Kansas City plays a vital part in the surveillance of cancer in our pediatric population. The Cancer Registry is a HIPAA-compliant confidential database comprised of malignant cancers, benign brain tumors and other specified benign tumors. The database is operated under the guidance of the Cancer Care Committee. Data collected, which includes diagnosis, treatment, recurrence and survival, is standardized for state and national comparisons.

Following each patient’s cancer status is a very important part of Cancer Registry data collection. Knowing outcomes of each cancer patient can assist with determining best treatment methods and long-term effects of cancer treatment. Therefore, follow-up letters inquiring about a patient’s cancer status are sent out yearly. Parents and older patients are encouraged to contact the registry by secure email at cancerregistry@cmh.edu to discuss follow-up.

During 2016, the Cancer Registry added 218 patients to the database. Of these, there were 193 patients who were diagnosed with malignancies and benign central nervous system tumors. There were 25 patients added to the registry as having benign reportable conditions treated by cancer specialists and surgeons. These conditions are collected at the request of the Cancer Care Committee for surveillance purposes and are not required to be reported outside our facility.
SARCOMAS
Sarcomas are rare but aggressive cancers that arise from cells of mesenchymal origin. These malignant tumors can arise from bone, cartilage, fat, muscle or vascular tissues. These cancers require an experienced multidisciplinary medical team of pediatric oncologists, surgeons (including general surgery, urology, ear nose and throat, and orthopaedic oncology) to adequately care for them.

While there have been significant improvements in all childhood cancer treatments since the 1970s, with childhood cancer mortality dropping by more than 50 percent since 1975, pediatric sarcomas remain a difficult group of cancers to treat.

Children’s Mercy Kansas City sees about 20 new patients on average each year with sarcomas. The survival data is closely compared to national statistics to ensure state-of-the-art care.

General information and updates on the three most common types of bone and soft tissue sarcomas seen in pediatrics follows.
Osteosarcoma is the most common bone tumor in children and adolescents, with approximately 450 cases in pediatrics and young adults in the United States per year. Osteosarcoma presents with pain and swelling around the tumor and often a limp if the tumor is in the lower extremities. Osteosarcoma most often occurs in the long bones around the knee, but can occur anywhere in the body. The diagnosis of osteosarcoma is made via biopsy. It is important that an experienced orthopaedic surgeon performs the biopsy, as this procedure is performed with the future resection in mind, and misplaced biopsies can compromise future local control.

Poor prognostic factors for osteosarcoma include a large size primary tumor, primary tumor sites in difficult-to-resect locations, and the presence of metastatic lesions in the lungs or other bones. After the administration of induction cycles of chemotherapy, the degree of tumor necrosis (less necrosis being unfavorable), and positive margins at the time of primary tumor resection are also poor prognostic factors.

Treatment of osteosarcoma requires aggressive chemotherapy with cisplatin, doxorubicin and methotrexate. Local control with surgery is crucial to a good outcome in osteosarcoma, as osteosarcoma is not sensitive to radiation therapy. Most patients with osteosarcoma will be good candidates for a limb-sparing approach. While amputation is uncommon, it is still necessary in some cases. Many options exist for custom prostheses in children, including magnetic expandable prostheses that allow for continued growth of the child.

The survival rate for localized osteosarcoma has improved from early studies to an overall survival rate of 65 percent at five years. About 20 percent of patients have metastatic disease at diagnosis, and the overall survival for these patients is approximately 30 percent at five years, although this is dependent on the location and the ability to resect metastatic sites. Efforts to intensify therapy for patients with poor prognosis have not improved survival. An international cooperative group trial intensified therapy for those with a poor response to upfront chemotherapy with the addition of ifosfamide and etoposide. This did not result in increased event-free survival or overall survival. Newer agents are in continual development for use in large cooperative trials.
The first day of kindergarten is one many parents remember—as both a happy and sad milestone. But Kambre Jo Konrade’s first day marked a milestone of a different kind. She was diagnosed with osteosarcoma—bone cancer.

That afternoon, the 5-year-old took a tumble off the monkey bars at school in Spearville, Kan., a small town northeast of Dodge City. During the evening, she complained that her leg still hurt. A trip to the ER led to an X-ray that initially seemed reassuring: no breaks or fractures. But the radiologist saw a grapefruit-sized mass above Kambre’s knee and forwarded the image to doctors in Wichita, Kan., and Kansas City. They confirmed the Dodge City doctors’ suspicions: tumor.

Kambre was referred to Children’s Mercy Kansas City for assessment and treatment. Her oncologist, Katherine M. Chastain, MD, Assistant Professor of Pediatrics, remembered how—early on—she was impressed with Kambre’s resilience.

“I could not believe this little girl had this huge tumor and very little pain,” Dr. Chastain said. “Just goes to show how tough she is!”

That toughness would be critical in facing her illness. Kambre was “too small with too many years left to grow,” her mother, Morgan, explained. That meant doctors couldn’t follow the typical procedure of removing the cancerous bone and installing an expandable rod.

“They didn’t make a rod small enough to fit her little leg nor with the potential to expand as much as she still could grow.” In addition, a specific margin of healthy bone must be removed to ensure all the cancer is eliminated—a critical necessity because recurrence yields less than a 30 percent survival rate. Plus, the typical procedure would have required additional major surgeries throughout Kambre’s life.

“The risks offset the benefits substantially,” Morgan said. Yet, the safer surgery for Kambre was also an extreme one: rotationplasty, a procedure in which surgeons remove the lower section of the leg and reattach the ankle and foot backwards to the thighbone. The ankle then acts as a knee joint for a prosthesis.

Dr. Chastain said, “Ensuring that rotationplasty was the best choice for Kambre was important, because we had to balance getting out a large tumor in a small child, plus making sure she had good function and no limitation in what she wanted to do going forward.”

Kambre proved immediately after surgery that “good function” would be an understatement in her recovery. The same day as the procedure, for example, she could move her toes on command.

“Normally that takes about two-plus days,” Morgan explained. “Kambre could also move her foot back and forth!” Later, on her first attempt with her prosthesis, Morgan said, “She did unbelievably well. It’s like she knew no different. Amazing is just what she does and who she is!”

The same could be said about the Children’s Mercy staff. “Children’s Mercy and all the providers we encountered along the way have been incredible,” Morgan said. “The specialty knowledge of her illness and willingness of her providers to listen to us and support us, as well as educate us, made us confident we were in the right place. Children’s Mercy knows kids and addressed the needs not only of the illness, but emotional, physical and mental, as well. We loved the family we became a part of while there!”

Kambre will continue to be part of that family for many years to come. “She has a good prognosis,” explained Dr. Chastain. “But osteosarcoma can still come back. So we will follow her a long time with regular scans.” Morgan added, “While you expect good care in a hospital, we continue to be humbled and beyond thankful for the nurses and doctors at Children’s Mercy.”

Kambre and her mom arrive for an appointment.

Lindsey Fricke, APRN, and Dr. Chastain strike a pose with Kambre during a recent visit.

KAMBRE KONRADE
Ewing sarcoma is the second most common bone tumor in children. It often presents in bones similar to osteosarcoma, but can also present in the soft tissues anywhere in the body. Ewing sarcoma most often presents with pain and swelling around the site of the tumor, and often is misdiagnosed for quite some time due to vague pain and the rarity of the tumor. Fever and weight loss can also occur.

Ewing sarcoma is diagnosed by biopsy, and there are several characteristic features of Ewing sarcoma that aid in diagnosis. First, Ewing sarcoma belongs to a group of “small round blue cell tumors” due to its characteristic appearance. CD99, a surface membrane protein, is expressed in most cases of Ewing sarcoma. There are also characteristic translocations involving the EWSR1 gene on chromosome 22. Most commonly this partners with the FLI1 gene on chromosome 11; however, other partners have been described.

Treatment for Ewing sarcoma involves intensive chemotherapy, surgery and/or radiation. Even if there is not metastatic disease seen on scans, we know that there is occult metastatic disease too small to be visualized with current imaging techniques. Therefore, chemotherapy is paramount to cure.

Chemotherapy uses five drugs (vincristine, doxorubicin, cyclophosphamide, ifosfamide and etoposide), in compressed cycles every two weeks. Local control of the primary tumor is also crucial, and can involve surgery or radiation therapy. Surgery is the preferred method of local control if the tumor can be resected with negative margins. If surgery is performed, the tumor will be examined for necrosis, which corresponds with the effectiveness of chemotherapy. Patients with a high percentage of residual viable tumor have a worse outcome than those with a large amount of necrosis.

Recent cooperative group trials showed improved survival when using compressed cycles (every two weeks) instead of traditional three-week cycles. Ongoing studies are looking at additional agents to the standard five-drug regimen in both localized and metastatic Ewing sarcoma to further improve survival.

In Ewing sarcoma the five-year survival rate has increased to 78 percent for localized tumors thanks to cooperative group studies. Metastatic disease is present in 25 percent of patients at diagnosis, and survival in metastatic disease is still poor with an event-free survival of approximately 28 percent.

**Ewing Sarcoma Overall Survival**

![Graph showing Ewing Sarcoma Overall Survival](image)
ALEXANDER GOODWIN
EWING SARCOMA
Maruska and Jeff Goodwin weren’t initially worried when their usually happy, precocious, 8-year-old son complained about pain in his leg. But then it began waking him at night and their parental instincts went on high alert. When Alex began limping and was in nearly constant discomfort, the Leicester, United Kingdom, couple went searching for help.

For seven months, they took their son from one doctor to another, from Leicester to Sheffield to Birmingham, but there was no definitive diagnosis.

Meanwhile, Alex’s health worsened. “He was rapidly losing weight, was always very tired, stopped attending school, stopped eating and was in constant, unbearable pain,” his mother said.

Finally, doctors re-evaluated the boy’s condition and referred him to a bone-tumor specialist. A biopsy confirmed what the parents had feared all along: cancer—specifically, Ewing sarcoma. Tests showed a tumor had destroyed Alex’s right hip and thigh bone. Alex eventually began chemotherapy, but by then his health had significantly deteriorated. Soon, doctors told his parents nothing else could be done. Surgery to remove the tumor would simply reduce the quality of time Alex had left. His mother and father should prepare to say goodbye to their little boy.

But Alex’s parents chose a different path, beginning with an online search for help. Their efforts led them “across the pond” to Children’s Mercy. And doctors here offered a much different perspective on the little boy’s illness.

In December 2016—11 months after initially seeking treatment for their son—the family flew to Kansas City. After reviewing his records, Katherine M. Chastain, MD, oncologist and Assistant Professor of Pediatrics, University of Missouri-Kansas City, said the team here could offer surgery and further treatment. “We wanted to give some hope that we could help,” she said.

Alex was immediately admitted to Children’s Mercy, and chemotherapy was restarted as the health experts assessed his condition. “His treatment was very efficient,” Maruska said. “We felt we were very well-informed of every step taken, something we weren’t used to in the U.K.”

In January 2017, surgeons in Kansas City removed Alex’s tumor and thigh bone. He received titanium versions of his femur and knee cap, followed by more chemotherapy and a unique radiation treatment. By July, his cancer was gone. That same month, doctors replaced his titanium femur with a telescopic version that could grow with him.

Alex headed home in August, but he’ll be returning every three months for the first year, and then continued follow-up for many years to come. Dr. Chastain will check regularly to ensure his cancer hasn’t recurred, and his telescopic femur will be incrementally extended.

“Alex’s case has been challenging because of the aggressiveness of his tumor and the extensive surgery he required,” Dr. Chastain said. “But he has done remarkably well.”

His parents see the same fortitude. Maruska said, “Alexander is getting stronger every day. We will forever be grateful not only to the medical professionals, but to the numerous friends we made. Kansas City will always feel like a second home.”

“The level of expertise and care we received was astounding,” she added. “We feel so fortunate to have come here.”
Rhabdomyosarcoma is a highly aggressive malignant tumor of mesenchymal origin. It often is associated with skeletal muscle, but can occur in locations that lack skeletal muscle, making the cell of origin elusive. It is the most common soft tissue tumor in children, although it is still overall a rare malignancy with approximately 350 cases in the United States per year. Rhabdomyosarcoma occurs in two distinct subtypes; embryonal RMS, and alveolar RMS. ERMS is the more common subtype and has a better prognosis than the alveolar subtype. The alveolar subtype occurs in approximately 25 percent of cases, and is often associated with FOXO1 translocations. Tumors that appear to be alveolar, but lack the characteristic translocation, have outcomes equivalent to those with the embryonal subtype.

Rhabdomyosarcoma is treated with chemotherapy and local control with surgery or radiation. Radiation is often preferred over surgery in rhabdomyosarcoma, as tumors in the head and neck or genitourinary system can be difficult to completely resect. Chemotherapy varies by risk group, but always includes a VAC backbone (vincristine, daunorubicin, and cyclophosphamide). Staging is complex and factors in the location or tumor, subtype (ARMS vs ERMS), size, metastasis and extent of the surgical resection.

Rhabdomyosarcoma is usually curable in most children with localized disease, with more than 70 percent overall survival for those in low and intermediate risk categories. Metastatic disease continues to be a challenge to cure, especially in those with alveolar rhabdomyosarcoma.

Pediatric sarcomas have seen great advances in survival in the last several decades, but there is considerable work yet to be done to improve survival, especially for those with metastatic disease. As we work to improve outcomes, we also strive to prevent side effects from the therapy we give. Survivors of childhood cancer may have therapy-related sequelae, including ototoxicity, cardiac toxicity, radiation side effects, and issues with prostheses. It is imperative that these children be followed in a long-term survivorship clinic such as the Children’s Mercy Survive and Thrive Clinic, to screen for late effects. Early detection can minimize complications and improve quality of life. Now with more and more children surviving their cancer and living into adulthood, transitioning to adult providers knowledgeable in these sequelae is increasingly critical to prevent or reduce later health complications. The combined program developed with the University of Kansas Cancer Center offers a seamless transition for our patients as they become adults.
PERSEPHONE DURAN
RHABDOMYOSARCOMA
Persephone Consuela (Suela) Duran had a better chance of being hit by lightning than developing rhabdomyosarcoma.

Suela was a 12-year-old when she began experiencing what seemed to be harmless, though uncomfortable symptoms.

Claudia, Suela’s mother, said frequent doctor visits became the norm when Suela began menstruating. “We knew something was wrong, because Suela’s periods were extremely heavy, and she was always cramping,” Claudia explained.

Suela’s pediatrician in her hometown of Salina, Kan., tried birth control pills and injections to lessen her symptoms. Blood tests and physical exams initially showed no cause. But, in early September 2013, a mass was discovered in Suela’s uterus. She was 15 years old.

Surgery at the Salina Regional Health Center removed the tumor, and it was sent for a pathology test. A week later, results confirmed the teen had embryonal rhabdomyosarcoma (ERMS). The protocol was for a hysterectomy and chemotherapy.

Rhabdomyosarcoma is a rare cancer; just four per million patients develop it before age 15. And, on average, only 350 cases occur in the United States each year in children under age 21.

Her parents were caught off-guard by the severity of Suela’s illness. She had been a healthy child, taking dance lessons and playing soccer over the years. “We weren’t prepared for our 15-year-old to have her uterus removed, a port put in and chemo for six months,” Claudia said. “We were scared and devastated.”

That specialized care included six months of weekly chemotherapy treatments. So, every Friday, as soon as Suela’s father, Johnny, got off work from his night shift at the local college, the family packed into the car for the 175-mile drive from Salina to Children’s Mercy. Claudia said the disease impacted her daughter’s life in many ways.

“She was sick and missed out on sports, visiting and enjoying her friends, and eating out. She had to wear a mask to school. Fevers were a concern, and she was sick to her stomach on Mondays after treatment and couldn’t attend school,” Claudia explained.

But the staff at Children’s Mercy sustained them through the fear and uncertainty. “Her treatment at Children’s Mercy was the best you could hope for and receive,” Claudia said.

Suela said Dr. Chastain was particularly reassuring when the teen had questions. “She made me feel at ease with her laughter and reassured me I would make it through,” Suela said. “I felt like she cared about the whole person. She let me know I would make it to college, and I did.”

Now a sophomore at Kansas State University, Suela is studying business and hopes to become a veterinarian. Dr. Chastain said her former patient had an excellent chance of achieving that dream.

“She has a very good prognosis,” Dr. Chastain said. “She’s already several years out with no signs of disease recurrence.”

Claudia said she knew her daughter got “the best medical care in the world,” adding, “Our child is alive and well today because of Children’s Mercy staff.”
Sarcomas are malignant tumors that arise from bone, blood vessels, cartilage, fat, muscle or other connective tissue. Although they are considered rare in general, they are occasionally seen in the pediatric population. They are many different types of sarcomas that originate from bone or soft tissue and can arise anywhere in the body, including visceral organs and the brain.

When pathologists receive a tumor specimen, they examine the tumor under the microscope, identify the type of sarcoma and determine its grade and extension into the body organs. Sarcomas are named according to the tissue of origin they resemble, e.g., a malignant tumor that resembles bone or where the cells are trying to produce bone is called osteosarcoma. The most common sarcomas in children are rhabdomyosarcoma (arising from skeletal muscle), osteosarcoma (from bone), and Ewing sarcoma (can arise from either bone or soft tissue).

Infantile fibrosarcoma occurs mainly in infants and young children. Rhabdomyosarcoma and Ewing sarcoma are considered high grade and can significantly affect the patient’s survival. Other sarcomas can be labeled as low, intermediate or high grade based on certain cellular characteristics. To determine the grade of the tumor, the pathologist has to determine the degree of tumor resemblance to cell of origin, estimate the density of tumor cells, identify bizarre-looking pleomorphic cells, count the number of cells in mitosis, and identify areas of necrosis. Histologic examination is also helpful to identify invasion of the tumor cells into blood vessels or extension outside the organ of origin. Pathologic examination can also confirm metastasis, i.e., seeding of tumor cells in the lymph nodes, lungs or other distant sites.

Sometimes the pathologist will have difficulty in determining the type of the tumor or in differentiating one sarcoma from the other. In these situations, additional studies are performed to determine the type of protein or DNA molecules the tumor cells are secreting. Identifying protein expression through immunohistochemical techniques is a common way to confirm the identity of the tumor. Molecular studies are also performed to identify genetic events that are characteristic for each type of sarcoma. The results of all the macroscopic and microscopic examination, immunohistochemistry and molecular tests (if available) are combined into a comprehensive pathology report that is sent out to the treating physicians and patients. To maintain quality of pathology operations, the tumor is frequently examined by more than one pathologist.
Over the last several decades, there have been remarkable advances in the surgical management of sarcomas. While some sarcomas can be treated with radiation, others require complete resection in order to achieve a cure. Resection of large tumors in a growing child or adolescent is extremely complex. When a child is diagnosed with a bone or soft tissue sarcoma, it is imperative that they have a specialized orthopaedic oncologist who is familiar with the unique problems that arise in children.

Orthopaedic oncologists provide a specialized approach to remove tumors and reconstruct the bones to allow for normal function and full mobility. Orthopaedic oncologists have done extensive training beyond a general orthopaedics residency, and are familiar with the unique needs of sarcoma patients. Bone tumors in children most commonly occur close to the growth plates, which then must be excised during their definitive surgery. This can result in severely impaired growth of that extremity. Resection of sarcomas in children requires thoughtful planning and innovative surgical techniques as they continue to grow to their adult height and to maximize their function.

The goal of surgery is to always completely remove the sarcoma. In the past, amputation was the most common option. However, with advances in prostheses for children, amputation is now a last resort. Our team commonly uses a non-invasive magnetic expandable prosthesis. This prosthesis contains a powerful magnet that can be activated to lengthen the prosthesis. This allows for growth, without the needs for repeated invasive surgeries.

Howard Rosenthal, MD, and the orthopaedic oncology team at the University of Kansas Sarcoma Center work closely with the medical Sarcoma Team at Children’s Mercy, as well as radiation oncology to provide a multidisciplinary approach to optimize care for pediatric patients with sarcomas.

The prognosis and management of sarcomas has made great strides in the past 20-plus years, thanks in part to the enhanced role of Radiology in the team management of these complex patients.

Radiology is part of the multidisciplinary team for sarcoma patients. Interpretation of imaging by the diagnostic radiologist is essential for initial staging, therapy planning, and long-term surveillance. The interventional radiologist can provide a minimally invasive method of lesion sampling as part of the diagnostic work-up and follow-up. In some cases, Radiology provides a treatment arm as well, utilizing image-guided tumor ablation or embolization techniques to augment traditional treatment methods.

Physical therapy plays a significant role as part of the multidisciplinary team to promote optimal recovery and return of function in children with sarcomas. Physical therapists work to develop individualized exercise programs that combine stretching and resistance exercises to help reduce fatigue, as well as improve mobility, safety and overall function. Physical therapy is very important after limb salvage procedures and amputation surgeries, working on post-surgical mobility training, strengthening, endurance restoration, pain management and education. Often, children will have activity restrictions after surgery including weight bearing precautions. Physical therapy teaches children how to maintain these precautions with use of assistive devices including walkers, crutches and canes. Physical therapy allows patients to learn how to use a new prosthesis correctly and in a safe environment, as well as promoting optimal limb function. Physical therapy may also recommend bracing or splinting to assist with range of motion, muscle weakness and function.
The Survive & Thrive Program began in 2009 and offers comprehensive medical and emotional care to childhood cancer survivors who are at least two years off treatment and five years from the date of diagnosis. The program began with a monthly clinic and has grown to four clinics per month with more than 250 survivors receiving care.

Childhood cancer survivors are at risk for health problems or late effects from their cancer and treatment. Late effects can be physical or emotional and typically appear in the second decade of life. The development of late effects may be influenced by the type of cancer, the treatment, age at diagnosis and genetic predisposition. An estimated 95 percent of childhood cancer survivors will develop at least one late effect at some point during their life. Late effects may be preventable or modifiable, which is why lifelong follow-up is important for all survivors.

Examples of late effects include hearing loss, heart dysfunction, infertility, organ dysfunction (i.e., restrictive or obstructive lung disease), endocrine dysfunction and development of a second cancer. In the Survive & Thrive Clinic, survivors are monitored for development of late effects according to the Children’s Oncology Group Long-term Follow-up Guidelines.

The Survive & Thrive team ensures diagnostic tests and labs are completed according to the guidelines and referrals are made to other specialists when necessary. The Survive & Thrive team works closely with health care providers in other specialties to ensure each survivor’s unique health needs are met. Specialists the team works closely with include endocrinology, cardiology and developmental and behavioral sciences.

In 2016, Children’s Mercy launched the Cardio-Oncology Program to better meet the needs of cancer patients at risk for developing cardiotoxicity (damage to the heart and vascular system).

Anthracyclines are a class of chemotherapy drugs used in many pediatric cancer treatment regimens. Anthracyclines, even in low doses, increase the risk of heart problems in cancer survivors. Radiation therapy that involves the heart or major vessels (vena cava and aorta) also increase the risk of developing heart problems.

The Cardio-Oncology Program offers specialized treatment that incorporates screenings by pediatric cardiologists during cancer treatment and after for survivors. Monitoring for and addressing cardiac concerns early can reduce the risk of severe or life-threatening heart problems. Examples of heart problems that may arise during and after cancer treatment include: heart failure, valvular heart disease, left ventricular function, elevated cholesterol, elevated blood pressure and arrhythmia. The collaboration with the pediatric cardiologists ensures survivors at risk for cardiac problems receive comprehensive screening, education and intervention as needed.

A visit to the Survive & Thrive Clinic includes a thorough physical exam, recommendations for long-term follow-up care, education on late effects of cancer treatment and how to maintain a healthy lifestyle. Assessments by a dietitian and social worker are included in the survivorship clinic visit to ensure all needs of the survivor are met. In conjunction with the hospital-wide Transition to Adulthood Program, preparation for transition to adult providers is incorporated into each visit once survivors reach 15 years of age. The Survive & Thrive team works with each survivor to teach skills to advocate for their health care needs and develop an individualized transition plan.

In addition to clinic, the Survive & Thrive team participates in various activities to raise awareness about the importance of ongoing follow-up care for survivors. The team participates in the KC Cares Walk and Tour de BBQ, and has also hosted educational conferences for survivors and their families. Along with the Regional Hemophilia Treatment Center, the Survive & Thrive team hosts the LAUNCH Transition Program for adolescents, young adults and their parents/caregivers. The goal of this program is to provide information and resources to facilitate smooth transitions not only in health care, but in other areas of life (education, career, money management and independent living).
Laboratory methods used at Children’s Mercy include gold standard conventional chromosome analysis, fluorescence in-situ analysis, microarray analysis, and select somatic mutation analysis. Chromosome analysis visualizes the entire genome to detect gain or loss and rearrangement of chromosomes. Microarray, a high-resolution analysis of the chromosomes, detects loss of heterozygosity, gain or loss, and unbalanced rearrangement of chromosomes. FISH analysis assesses the status of specific genes, while somatic mutation analysis detects changes within genes. Each of these technologies offers a different assessment of the tumor and together provide the most complete picture of the genetic changes that drive the tumor’s growth. Knowledge of these genetic changes informs therapeutic choices.

Laboratory analysis reveals unique genetic changes that are present in every tumor. Findings provide information to aid in diagnosis and subtyping of each tumor and contributes information for therapeutic management. The status of important genes is determined: fusion of two genes in an abnormal way can cause cell growth; gain of too many copies of a gene encourages cell growth, while loss of certain genes takes away control of cell growth.

Figures 1-3 demonstrate subtypes of rhabdomyosarcoma and their genetic differences.

Fig 1. (above) Alveolar rhabdomyosarcoma (ARMS) is characterized by gene fusions in ~80 percent of tumors. PAX3-FOXO1 fusion, found in ~60 percent of ARMS, is shown by the karyotype as a reciprocal translocation of material between chromosome 2 long arm and chromosome 13 long arm. There is gain of an extra copy of the abnormal chromosome 13.

Fig 2. (left) Alveolar rhabdomyosarcoma (ARMS) with a PAX7-FOXO1 fusion is seen in ~20 percent of tumors. The karyotype shows a reciprocal translocation of material between chromosome 1 short arm and chromosome 13 long arm, which results in the PAX7-FOXO1 fusion. The tumor has 91 chromosomes and two copies of the abnormal chromosome 1.

Fig 3. (left) Embryonal rhabdomyosarcoma (ERMS) commonly shows a hyperdiploid karyotype without translocations or gene fusions. This tumor has 59 chromosomes with gain of extra copies of chromosomes 1q, 6, 7, 8, 12, 13, 19, 20, and 21.
Although most children and adolescents diagnosed with sarcomas are cured with standard therapy, unfortunately there are some who will relapse or who do not respond to treatment. As initial treatment often includes surgery and/or radiation therapy along with intensive chemotherapy, children who are not cured are left with limited options.

Fortunately, scientific research is making great strides toward improving our understanding of cancer biology. This increase in knowledge is being translated into innovative therapies that are improving the lives of patients with cancer. Many of these new medications are designed to specifically target cancer cells or harness the power of the immune system to help kill cancer cells.

The Experimental Therapeutics in Pediatric Cancer Program brings many of these new, exciting drugs to patients at Children’s Mercy. For children with sarcomas that are not cured with initial therapy, there are a number of phase 1 and 2 research trials that provide access to the newest and most promising treatments. As members of the Children’s Oncology Group (COG) and the Beat Childhood Cancer consortium, Children’s Mercy is part of truly groundbreaking research, striving to transform the remarkable amount of new information about how cancer cells function at a molecular level into new therapies.

The Experimental Therapeutics Team at Children’s Mercy includes four physicians, an advanced nurse practitioner, a social worker and four outstanding clinical research coordinators. They work together to ensure that our patients are getting the best new treatments in the safest way possible.
In some cases, pediatric sarcomas are associated with inherited mutations in cancer-causing genes. There are several genetic changes that are known to increase the risk of sarcomas in children. These include mutations of the TP53 gene, which causes Li Fraumeni syndrome, the RB1 gene, which increases the risk of osteosarcoma, and the APC gene, which is associated with desmoid tumors, as well as many other rare genetic changes. In each of these conditions, the child may be otherwise healthy prior to the discovery of the sarcoma. A strong family history of cancer, unusual types of cancer, multiple cancers in one person, or adult-onset cancers in childhood can be clues that a family cancer syndrome may be present. The Center for Genomic Medicine at Children’s Mercy has developed a specialized, comprehensive DNA sequencing test to detect cancer-causing mutations in patients and their relatives. Our genetic counselor meets with families to discuss the test results. At-risk patients are followed in our Cancer Predisposition Clinic for health surveillance and specialized testing. For more information about the genetic testing or the Cancer Predisposition Clinic, contact, the Division of Hematology/Oncology/Bone Marrow Transplantation at Children’s Mercy Kansas City.
Multidisciplinary care is integral to the overall outcomes and well-being of our patients. Outside of medically directed care, patients and families have many other needs that are addressed by our Family Care Team (FaCT). Regular FaCT rounds and collaboration ensures that we meet all physical, developmental, emotional, educational and spiritual needs. The Family Care Team is available to assist from point of diagnosis through the completion of treatment and beyond for patients with sarcomas or any other cancer.

The Child Life team consists of child life specialists and a patient activity assistant who is also the handler of the facility dog on staff who works on the inpatient unit. The team works collaboratively to support the psychosocial and developmental needs of children and families. Child life specialists are trained professionals who help children cope with the stress and uncertainty of illness and hospitalization. Child life specialists work to ensure life remains as normal as possible for children. Child life specialists explain and teach patients about medical procedures, coping skills and other health care experiences. As advocates of family-centered care, child life specialists work in partnership with the medical team to meet the unique emotional, developmental and cultural needs of each child. Patient activity coordinators provide play activities and facilitate positive and safe play environments. They promote patient engagement in play programs, volunteer interactions and special events.

Clinical social workers are master’s level licensed professionals working as part of the primary team to provide comprehensive and compassionate family-centered care. Social workers understand that any change in the child’s health can alter a family’s life in many ways, and are trained to provide a thorough assessment and address the ongoing needs of the patients and families. Social workers can help with therapeutic support including adjustment to illness, crisis intervention, development of coping skills, family concerns, end-of-life, and bereavement; care planning including education on advance directives, school concerns, legal issues, transition to adult care, and end-of-life concerns; and community/resource referrals to assist with financial concerns, transportation and lodging needs, support and mental health referrals. Every patient has an assigned clinical social worker who follows the patient and family through diagnosis, treatment, relapse, survivorship or bereavement.

The Parent-to-Parent Program offers support and comfort to families through the use of specially trained parent volunteers and a clinical social worker. There are many services offered through the PTP program including parent volunteers available to share, listen and support our current parents; two stocked parent rooms that offer weekly dinners, breakfasts, therapeutic and educational activities and a safe place to unwind while a child is an inpatient; “care bags” for families upon unexpected admissions to help ease some burden of a hospital stay; and new parent journals. The Parent-to-Parent program also offers an extensive bereavement follow-up program that supports families for approximately 13 months after a child’s death. We have successfully introduced social media into our bereavement follow-up program. PTP has worked closely with a number of local organizations, as well as the Children’s Mercy Cancer Center Auxiliary, and has established ongoing philanthropic support of the parent rooms to serve the increasing needs of our inpatient families. The program was highlighted at the 2017 Association of Pediatric Oncology Social Workers conference.
The Adolescent and Young Adult Program is designed to support patients receiving treatment for cancer or blood disorders. The team of providers includes a clinical social worker and child life specialist who work in collaboration with other disciplines toward the goal of improving the quality of care for the AYA population. Recent accomplishments include the development of a teen unit and teen room on the inpatient floor; a formalized peer mentoring program; additional programming and education around fertility preservation; and improvements to transitioning to adult care. Ongoing projects include the Hematology/Oncology Teen Advisory Board; Teenapalooza events to promote peer interaction; and education and support.

There are two dedicated psychologists to assist patients and families with coping with the diagnosis and treatment of sarcoma and other cancers. They are available to meet with patients and their families, both while hospitalized and when outpatient. In addition to clinical therapeutic services, the psychologists are also able to complete neurocognitive evaluations to assess any impact of the cancer or the medical treatment on brain functioning and to assist with school re-integration and planning.

The chaplains regularly provide spiritual and emotional support to patients and families during the course of a child’s illness and beyond. Providing tailor-made rituals for patients and families at the time of significant events like bone marrow transplant is another way a chaplain provides support. At the request of the family, the chaplain can contact a family’s own clergy person/spiritual leader. For families who live outside of the Kansas City area, at the request of the family, the chaplain contacts a local leader from the family’s faith tradition to provide additional support. The chaplain provides education about the spiritual resources that are available within the hospital, such as the activities in the Lisa Barth Chapel like Sunday worship, concerts and celebrations from various faith traditions. The chaplain participates in team meetings. Providing support to the staff is another important role of the chaplain.

Music therapy services are offered to patients and families at bedside to address the specific needs of individual patients. Music interventions are designed after an assessment of need and generally involve the use of both live vocal and instrumental music, as well as technology. Goals may include but are not limited to the reduction of pain or anxiety; increased self-expression, movement, or relaxation; and the support of developmental skills. Patients are encouraged to take an active role in making music and learning how to use music as a helpful and fun tool.

An on-site school teacher works with patients primarily on the inpatient floor with some availability in clinic as needed to assist with the challenge of keeping up with school work while a patient is undergoing treatment. Our school teacher is able to communicate directly with the child’s school to get current assignments and also to advocate for the patient’s needs once they return to the school setting.
RESEARCH FOCUSES ON MORE EFFECTIVE SARCOMA THERAPY

Medical specialists at Children’s Mercy do more than treat children’s illnesses. They also research ways to make treatments as effective as possible. Among these are two physician scientists leading this effort in pediatric sarcomas work at Children’s Mercy.

Katherine M. Chastain, MD, Pediatric Hematologist Oncologist and Director of the Soft Tissue and Bone Tumor Program, is studying how pediatric solid tumors respond to treatment. “I want to better understand and develop treatments for solid tumors and other rare tumor types,” she said.

Glenson Samuel, MD, Pediatric Hematologist Oncologist, is attempting to determine whether pediatric sarcoma cells release nanosized molecules, exosomes, into the circulation. These molecules could be used as markers to monitor pediatric sarcomas.

“Exosomes may contain characteristics that are similar to their originating tumor,” Dr. Samuel explained. “Our research will help us better understand how sarcomas work and can be monitored throughout therapy.”

An aspect of this exosome research has led to a partnership with the Genomic Medicine Center at Children’s Mercy. Other research focuses on targeted therapies for progressive or recurrent pediatric sarcomas patients, specifically on the molecular mechanism by which cells multiply.

For both physician scientists’ studies, samples are collected from consenting patients who participate to help future patients. Dr. Chastain’s study takes cells from the tumors at the time of their initial diagnostic biopsy/resection.

“We then use a new way of growing the cells in the lab and to test new treatments,” such as different drugs or drug combinations, she explained. “We will also test the tumor cells before and after treatments and see what differences we can find. The child’s tissues will be stored in a way that allows cells to grow and multiply,” she added. These multiplying cells may give rise to cell lines, which can be kept alive for many years and used for multiple future studies.

Dr. Samuel’s exosome study uses blood samples from newly diagnosed and recurrent patients. Samples are collected throughout therapy to correlate research findings with standard methods of monitoring pediatric sarcomas.
BONE AND SOFT TISSUE SARCOMA PROGRAM

Sarcoma accounts for about 15 percent of all childhood cancers. Each year, Children’s Mercy treats about 20 children with new diagnoses of bone or soft tissue tumors. The Bone and Soft Tissue Sarcoma Program at Children’s Mercy is led by Katherine M. Chastain, MD, who completed fellowship at Memorial Sloan-Kettering Cancer Center. The program includes: Orthopaedic Surgery (Howard Rosenthal, MD), Radiation Oncology (Vickie Massey, MD), Rehabilitative Medicine (Kimberly Hartman, MD), Pediatric Oncology, Pathology, Interventional Radiology and Radiology. Our goal is to provide seamless care coordination with a multidisciplinary tumor board and enhanced collaborative research across disciplines.

The Bone and Soft Tissue Clinic allows patients to receive all services on one campus. Commonly treated diagnoses include osteosarcoma, Ewing Sarcoma, rhabdomyosarcoma and non-rhabdomyosarcoma soft tissue sarcoma.

LEUKEMIA AND LYMPHOMA

The Leukemia and Lymphoma Program includes experts in the diagnosis and management of hematologic malignancies in children and young adults. The program is a collaborative effort dedicated to delivering state-of-the-art clinical care and to generate innovative research. Members include faculty from the section of Oncology, Hematopathology, Cytogenetics and the Genomic Medicine Center. Comprehensive patient care meetings occur monthly. Cases are reviewed and research discussed. Members are actively involved in the development of clinical trials for leukemia and lymphoma on a national and international level through the Children’s Oncology Group and other clinical research consortiums.

NEURO-ONCOLOGY PROGRAM

The Children’s Mercy Cancer Center Neuro-Oncology Program is led by Kevin Ginn, MD, with a primary focus of providing access to cutting-edge cancer therapy for children in the Kansas City region with brain and spinal cord tumors. Central nervous system tumors remain one of the leading causes of cancer-related death and morbidity. These patients benefit from the individualized care plans developed by multiple subspecialists available at Children’s Mercy. Our frequent tumor board allows in-depth discussion regarding each patient, ensuring proper planning for improved patient care. Our involvement in national consortiums such as the Neuroblastoma and Medulloblastoma Translational Research Consortium and the Children’s Oncology Group allows us to provide enrollment on clinical trials for both new and relapsed patients. Exciting research collaborations through the Midwest Cancer Alliance Partners have resulted in funded research investigating new therapies for glioblastoma and atypical teratoid rhabdoid tumor, which are two of the most devastating tumors in pediatrics. The goal of the Neuro-Oncology Program continues to be comprehensive care and cutting-edge therapy provided close to home.

HISTIOCYTOSIS PROGRAM

The Histiocytosis Program provides a comprehensive setting for care of a rare disease. The experience and knowledge of a pediatric hematologist/oncologist, J. Allyson Hays, MD, provides current and inclusive clinical care. The Histiocytosis Program also collaborates with pediatric orthopaedic surgeons, endocrinologists, dermatologists and pathologists familiar with the rare diseases of Langerhans cell histiocytosis, hemophagocytic lymphohistiocytosis, sinus histiocytosis with massive lymphadenopathy/Rosai Dorfman, juvenile xanthogranulomatous disease and Erdheim-Chester disease.
SPANISH LANGUAGE PROGRAM

The Spanish-speaking Hematology/Oncology Program’s primary mission is to bridge the gap in health care disparities among Hispanic patients and families with limited English proficiency. We are dedicated to providing comprehensive medical care to our patients with an emphasis on language-concordant medical services and an understanding of socio-cultural differences toward illness and health care. This clinic provides patients and families a full line of clinical services in Spanish. This includes written educational materials, medication calendars, medication lists and appointment schedules. The clinical implications of care for Spanish-speaking patients with childhood cancer are noted in published literature. Acute lymphoblastic leukemia is one of the most curable childhood cancers with an overall survival rate for Caucasian children of approximately 85 percent. The outcome for Hispanic children is approximately 75 percent. The exact reasons for this difference are unknown. A few small studies have implicated genetic differences in the leukemia cells themselves. Others have suggested language barriers and socio-cultural differences. We see our Spanish language program as a starting place for important research that will seek to discover the reason for differences seen in this population. Through our partnering with our clinical pharmacology and genomics programs, research into these differences has been developed and launched, with the intent to partner with other centers that serve large numbers of Hispanic children, including several children's hospitals in Mexico. We also see this as a means to develop clinicians skilled in the care of children whose primary language is not English.

adolescent and young adult program

The Adolescent and Young Adult Cancer Program was developed to improve outcomes by focusing on increasing awareness of the unique needs of AYA patients, improving compliance with treatment regimens and follow-up care. Addressing the psychosocial, educational and occupational needs of patients on and off treatment to improve overall quality of life is also a major focus of the program. At Children’s Mercy, we offer patients in this age group access to clinical trials through the Children’s Oncology Group. Members of the program are also available to discuss cases with adult oncologists treating patients with pediatric cancer who due to age are unable to receive treatment at Children’s Mercy. We will gladly help guide their therapy and provide psychosocial support to the families.

Children’s Mercy Tumor Bank

The Children’s Mercy Tumor Bank is a resource to clinicians and scientists who study the biologic basis of cancer in children. The biorepository consists of a collection of blood and tissue, donated by patients with cancer and cancer-related diagnoses. Information about each patient’s disease and response to treatment are also stored within the biorepository. The rights and privacy of participants in the biorepository are protected by a research protocol approved by the Children’s Mercy Institutional Review Board. The biologic samples and clinical data are accessible to researchers at Children’s Mercy, its partner institutions, and the greater scientific community.

Cancer Genomics

The Cancer Genomics Program is working to bring cutting-edge genomics research into everyday patient care. While cancer cure rates at Children’s Mercy are excellent when compared with national averages, we are always striving to improve. Genomic medicine studies are providing new clues into the causes of cancer and will help design better treatments.

Genomics studies of cancer cells can give us critical information about the genes and pathways that are active inside the tumor. The field of cancer genomics is brand new, but growing rapidly. Children’s Mercy is a worldwide leader in genomic medicine and has received international recognition for our ability to provide whole genome sequencing for critically ill neonates within a few short days. The same technology can be used to provide genomics information to our cancer patients quickly when it is needed to guide treatments.

Currently, the Cancer Genomics Program is enrolling patients in research studies of pediatric cancer. Our vision is to bring genomic medicine to every cancer patient at Children’s Mercy. We work in partnership with the Children’s Mercy Genomic Medicine Center.
LIVER TUMOR PROGRAM
The Liver Tumor Program includes oncology, hepatology, surgery and liver transplant services. The team works to give comprehensive care to children with liver cancer. Every patient's treatment plan is discussed with all of the disciplines. The coordination of care begins prior to diagnosis and continues even after treatment has been completed.

IMMUNOTHERAPEUTICS PROGRAM
The Cancer Immunotherapeutics Program promotes innovative basic and translational investigation designed to support and launch clinical trials targeting pediatric and adult malignancies. The program supports local investigator-initiated cancer-directed cellular-therapeutics trials at Children's Mercy and the University of Kansas Medical Center and participates in pharmaceutical-company sponsored trials of cellular therapeutics and complex biologics. Children's Mercy is one of the initial U.S. cancer centers to study and now offer the ground-breaking chimeric antigen receptor T (CAR-T) cell therapy for leukemia.

PATIENT AND FAMILY RESEARCH
The Patient and Family Research Program focuses on individual and family development, as well as issues that occur across the treatment trajectory that could compromise individual and family well-being. This includes supportive care, symptom management and psychosocial needs for all members of the family. The patient and family research program works in conjunction with other programs across the hematology/oncology/BMT spectrum in collaboration to promote positive patient and family outcomes.

EXPERIMENTAL THERAPEUTICS
The Experimental Therapeutics in Pediatric Cancer Program provides access for patients to new and innovative cancer treatments, placing Kansas City at the heart of national and international research efforts that are impacting the lives of children with cancer everywhere. We have 17 Phase I and II trials available for relapsed or refractory cancer. The Experimental Therapeutics team includes four physicians, each with their own specific area of interest including solid tumors, blood cancers, cancer genomics, clinical pharmacology and neuro-oncology. The team also includes a full-time advanced practice nurse practitioner and four dedicated clinical research coordinators.

As the only pediatric tertiary care hospital in the region, Children's Mercy cares for the vast majority of children in the area diagnosed with cancer. The number of children treated at our Cancer Center continues to rise, with an average of over 200 new cancer diagnoses a year. Children's Mercy serves as the pediatric partner for the University of Kansas Cancer Center's National Cancer Institute. This relationship allows for increased resources and access to clinical trials, bringing cutting-edge cancer therapy to our patients. Children's Mercy is an active member of the Children's Oncology Group, an international consortium that develops and operates clinical trials in childhood cancer. We are also a member of the Beat Childhood Cancer Consortium (formerly NMTRC–Neuroblastoma and Medulloblastoma Translational Research Consortium). We partner with pharmaceutical companies to run several industry-sponsored clinical trials to make sure our patients have access to novel therapies. In addition, the Experimental Therapeutics program has a Precision Medicine Research Core that encompasses the research pillars of cancer genomics and clinical pharmacology to develop locally developed trials in pediatric cancer.

In a given year, Experimental Therapeutics treats 15 to 20 children on our clinical trials. In addition to local and regional patients from the Kansas City area, we receive a number of outside referrals from other centers including Wichita, St. Louis, Oklahoma, Colorado, Iowa, Arkansas, Illinois and Texas. We are one of only a handful of centers currently treating children with difficult-to-treat leukemia with CAR T-cells, a revolutionary new therapy that uses a patient's own immune system to kill cancer.
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