Saving kids with science: How clinical trials are changing pediatric cancer care

by Jeremy Manier
Moments after Desiree Thomas learned that her young daughter’s life was in danger from an advanced form of cancer, she began weighing whether to enroll the child in a clinical trial.

The neuroblastoma afflicting her daughter, 3-year-old Madison Booker, had already spread far within the left side of the girl’s body by the time it was detected in 2007. It was a Stage 4 tumor, the most difficult to treat. The cancer specialists at the University of Chicago Medical Center told Thomas her daughter had less than a 40 percent chance of being cured, but aggressive treatment could help her lead a reasonably normal life.

Like many parents of pediatric cancer patients, Thomas agreed to let her child take part in a clinical trial. She knew some parents who felt uneasy about putting their children in any kind of experiment, but Thomas said she decided the study could enhance her daughter’s care and pave the way for children in the future.

“I felt that somebody else had (been) willing to put their kids in a study in order for Madison to get the treatment she got,” said Thomas, who works at a preschool on Chicago’s South Side. “I needed to do my part.”
Although Thomas had no way of knowing how the trial would turn out, her choice may have improved Madison’s outcome. The antibody treatment she received has proven superior to previously available therapies—information that researchers could never have obtained without young patients such as Madison.

It might seem like a gut-wrenching decision for parents, but putting kids in clinical trials is the norm at most pediatric oncology centers. In fact, far more children take part in cancer trials than adults. Nationwide, about three-fourths of children with cancer are treated in clinical trials, compared with less than 5 percent of adult patients.

That difference may help explain the high survival rates in recent years for children with cancer, experts believe. All patients in clinical trials must adhere to precise treatment protocols, with routine monitoring from outside medical experts. The nationwide trend of putting kids with cancer in such trials may help children get high-quality care.

“We really feel that clinical trials provide state-of-the-art therapy for children with cancer,” said Susan Cohen, MD, who treated Madison and is director of clinical research in the Section of Pediatric Hematology and Oncology at the University of Chicago Comer Children’s Hospital.

Kids with cancer represent a unique group of patients—they are vulnerable, yet strikingly resilient. Their good physical condition can make them ideal patients for clinical trials, but their young age means that doctors and parents must navigate medical and ethical concerns that seldom arise with older patients.

The first challenge is obtaining informed consent for a child to take part in a trial. Minors must have a parent or guardian go through the consent process, which often begins virtually as soon as a child is diagnosed.

In the case of complex procedures that require prolonged courses of therapy, doctors and nurses may spend hours talking about the clinical trial with parents over the course of several visits, said John Cunningham, MD, chief of the section of Hematology and Oncology at Comer.

“We usually spend up to three hours discussing the clinical trial before we ask the parents to decide whether to participate,” said Cunningham, who also runs the pediatric stem cell transplant program at the Medical Center.

Such investments of time contribute to the high participation rates at the Medical Center and other hospitals. More than 90 percent of parents accept the offer to put their children in clinical trials here, which can contribute to the quality of care that patients receive, Cohen said.

“When you’re on a clinical trial, if the protocol says you’re supposed to get chemotherapy on Monday, you get the chemo on Monday,” Cohen said. “There are a lot more people who are watching your back.”

Trials are closely monitored, she said, and studies will end early if doctors observe problems—or if a new treatment is much better than previous treatments.

For Desiree Thomas, any concerns about her daughter’s clinical trial were far outweighed by the frightful progression of the girl’s tumor. She said the growth on the left side of Madison’s body felt like a small lemon from the outside, but tests determined that it was “about the size of a 4-pound turkey breast.”

“What worried me was that she’s such a tiny thing,” Thomas said. That observation drew an instant objection from Madison, now 4 years old.

“I’m a big girl,” Madison said. “Who you telling I’m a baby?”

Thomas responded gently, “Well, you know, you’re tiny.”

“I’m not tiny!” Madison said. “Just Madison.”

Madison’s bravado about her toughness may be justified. Despite their seemingly vulnerable age, children like Madison can tolerate and survive difficult courses of chemotherapy and radiation, experts say—often in more intense doses than adult patients could withstand. A major reason is that children usually have the benefit of fit and healthy organs, unlike older patients whose bodies already have sustained a lifetime of wear and tear.
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“Right now, with the types of therapies we have available, we actually see kids tolerate chemotherapy and other cancer treatments much better than adults,” Cohn said. “If you’re dealing with someone who’s elderly and has cancer, it’s much more difficult to give them the kinds of aggressive treatment that we often use. Elderly patients often have organ dysfunction, and many can’t tolerate the side effects of these therapies.”

Cancer trials for children have helped drive advances in the care of adults with cancer, experts say. The chances of surviving acute lymphoblastic leukemia, the most common form of pediatric leukemia, have improved dramatically since the 1970s—from a survival rate of about 30 percent to more than 90 percent today. The advances in chemotherapy techniques that led to that improvement have affected how adults with leukemia get treated as well, Cunningham said.

Controlled studies are the only way to discover which treatments work best, but the logistical challenges in putting together a pediatric trial can be daunting. About 12,500 kids get diagnosed with cancer each year, which means no single medical center can amass a sufficient number of patients to conduct rigorous studies comparing treatments. If the number of children in a study is too small, researchers can’t use statistical methods to determine the significance of a drug’s effect or the difference between two treatments.

One solution is the Children’s Oncology Group, a cooperative organization that allows centers across the country to pool their scholarly resources and collaborate on large studies of children with cancer. Virtually all of the pediatric oncology clinical trials in the U.S. are coordinated through the group, which allows a much faster pace of discovery than would be possible for medical centers working in isolation.

The relatively small number of pediatric cancer cases also increases the motivation for doctors to recruit families for trials. Each child represents a precious chance to increase a trial’s size.
to the point where researchers can learn something useful about the disease or treatment. And unlike some clinical trials, no patients receive placebo treatments. Results from the new cancer treatments are measured against treatments that were found to be the best in previous clinical trials.

"The emphasis on conducting clinical trials and doing collaborative research really is ingrained now in the training of pediatric oncologists," said Stephen Skapek, MD, an associate professor of Pediatric Oncology at the Medical Center. "And a lot of it has to do with the parents. A lot of parents come in with the mindset that they really want a clinical trial for their child, because they want to get the most up-to-date therapy."

Desiree Thomas said her daughter's diagnosis with neuroblastoma launched her into a long process of education about the disease and the trials that were available. Cohn described the stages of chemotherapy that Madison would be going through and said she believed there would be a trial available for the girl after the initial rounds of chemo were finished. Cohn said she would have placed Madison on a trial immediately, but by chance there was no study open to new patients at that time, so the girl received chemotherapy according to protocols used in the most recently completed trial.

Madison, who was diagnosed in September 2007, lost most of her hair to the chemotherapy within weeks, Thomas said.

"I was braiding her hair, and it started coming out in big clumps," Thomas said.

That was the start of many rounds of therapy for Madison's advanced cancer. Next came surgery, followed by high-dose chemotherapy, stem cell transplant and radiation. Doctors also gave Madison retinoic acid, which previous clinical trials had shown to help cancer patients recovering from transplant therapy.

But even after those successful rounds of treatment, her oncologists knew Madison was not out of danger. Kids with high-risk neuroblastoma have about a 60 percent chance of relapsing after treatment, so researchers are always looking for ways of attacking any remaining cancer cells. Cohn recommended that Madison be enrolled in a clinical trial of an experimental antibody. She would receive an infusion of antibodies designed to target any lingering cancer cells and train Madison's immune system to attack those cells on its own.

"The hope is that this antibody will stimulate the immune system to destroy the neuroblastoma cells, similar to the way the body attacks viruses and bacteria that cause infection," Cohn said.

That was a reasonable hope based on early phase clinical studies, though before the trial no one knew if the antibody would be effective for patients like Madison. But in March, an outside monitoring board concluded that adding the antibody treatment significantly raised the chance of survival for neuroblastoma patients who already have received the standard therapy.

Of course, no one knows ahead of time which trials will be successful. The uncertain outcome of such treatments can add to the anxiety for parents and medical professionals alike. Skapek said some doctors choose not to specialize in pediatric oncology because of the emotional toll of striving to save vulnerable children who may not survive.

"It's not for everybody," Skapek said.

Yet Skapek said some of his most rewarding experiences as a physician have happened while caring for children who ultimately died from their disease. He said those young patients and their families have taught him more than he can describe about why his work is so important.

"I treasure the opportunity to help people, even in that setting," Skapek said.

Sometimes young children with serious illnesses take comfort in the idea that, by taking part in a clinical trial, they could help other kids in the future, experts say. Rosa Fuentes, a Comer nurse in Pediatric Oncology, said the chance to help others can sustain families in difficult times.

"We hear over and over again from families that their children are doing well because other children participated in trials, and this is their way to give back," Fuentes said.

Although the news from Madison's trial is encouraging, it's not a guarantee of a good outcome for individual patients. No one knows yet how Madison Booker's experimental treatment will turn out, though she's in remission and so far the signs are good. The girl spent so much time in the hospital that now she misses the doctors and nurses at the Medical Center, said Thomas, Madison's mother. Thomas said it helps to know that Madison also left a lasting impression at Comer through the research she helped advance, and the friendships she made.

"There's not a person Madison meets that she does not touch. She touches you in places you didn't think existed."