WALL STREET JOURNAL: By Amy Dockser Marcus

Dillon Papier was patient No. 2 in the cyclodextrin drug trial that began in January at the National Institutes of Health in Bethesda, Md. The Papier family lives about an hour away in Frederick, Md.

The 10-year-old boy didn't like hospitals, but he was always excited to see Forbes D. Porter, who was in charge of the trial. Dillon enrolled early in Dr. Porter's ongoing study of NPC disease. At appointments, Dillon shouted down hallways, "Paging Dr. Porter," and ran into the doctor's arms.

Dillon carried his bat, ball and glove everywhere. His father, Mark Papier, a high-school social-studies teacher and baseball coach, had shared his passion for the sport.

As the disease progressed, Dillon lost coordination but his Little League teammates asked that he stay on the team. At the start of games, the coach pitched to Dillon and the boy ran to first base.

In 2007, the Baltimore Orioles heard about Dillon's story and invited him to spring training. Over the years, Dillon grew close to second baseman Brian Roberts. They sometimes sat in the dugout together and talked.

After Dillon's diagnosis, the family started raising money for NPC research, work that gave them a sense of some small control over the fatal disease.

The owner of Foster's Grille, a family restaurant in town, had a suggestion: A portion of the dinner proceeds one night could go to the National Niemann-Pick Disease Foundation.

The first dinner was in 2008 and it turned into a regular event on the first Monday of the month. High-school baseball players brought their girlfriends. Friends from Little League showed up with their parents. Neighbors and classmates

stopped on the way home from work or from after-school activities.

The surgery to implant a catheter in Dillon's head to deliver cyclodextrin was scheduled a few days after the first Monday in February this year. Dr. Porter's wife suggested some of the scientists meet at Foster's for dinner.

Charles Vite, who ran the NPC cat colony, drove from Philadelphia with his wife. A baby sitter stayed late with the couple's three children.

Steven U. Walkley, the scientist from the New York City lab, drove five hours, ate dinner, then drove five hours home to be at work the next day.

No one knew if the drug would have the same remarkable effect on Dillon as it had on lab animals. The evening, Dr. Walkley said, was "a gut-check moment, for the parents and the scientists."

Eight days later, on Feb. 12, a medical team crowded into a hospital room at the NIH to give Dillon his first dose.

Nurses wore two pairs of gloves and dressed head-to-toe in surgical gowns and caps. They cleaned the skin that covered the catheter on Dillon's skull. A line of stitches on Dillon's partially shaved head marked where the boy's scalp was opened to implant the sterile plastic tube.

Dillon, dressed in a red, long-sleeve T-shirt and black sweatpants, was awake. He watched a video of "High School Musical," and talked with Dr. Porter and his parents.

Cards from classmates hung on the walls. A friend named Brad sent a drawing of a baseball diamond and a scoreboard: Dillon 100, Brad 0.

The cyclodextrin came as a clear liquid in a vial that was drawn with a syringe and injected into the tube that went to Dillon's brain.

"Starting the medication," a nurse said.

The Papiers accompany their son into surgery to implant the catheter in his brain.

The Hempels also received permission from the FDA for Addi and Cassi to get the same type of catheter used in the NIH trial, a device known as an Omayya reservoir. The catheters were implanted by surgery in the first week of April.

Four days after arriving home from the hospital, Cassi started vomiting. She stopped drinking and eating. At a hospital emergency room in Reno, a CT scan showed bleeding in her brain.

A helicopter prepared to airlift Cassi to a hospital in Oakland, Calif. Chris Hempel asked one of the paramedics if she could fly with them. She couldn't; more weight would make it difficult to navigate over the Sierra Nevada range.

The Hempels left by car without packing a suitcase and arrived four hours later. Ms. Hempel's sister in California drove to Oakland to meet Cassi at the hospital's helicopter pad.

Dr. Porter heard the news and sent the Hempels an email: "Thoughts and prayers are with you and with Cassi."

Cassi was bleeding where the catheter was inserted, and the growing clot was preventing brain tissue from receiving oxygen. She couldn't move her left side. Doctors removed the catheter in emergency surgery.

Hugh and Chris Hempel stayed with her at the hospital for six weeks. A friend packed a bag with clothes and drove it to Oakland. Ms. Hempel's parents stayed with Addi in Reno. The Hempels took turns going home to visit.

Doctors were baffled. Implanting the catheters, frequently performed by neurosurgeons, is a relatively low-risk procedure.

Cassi's doctors considered several possibilities. Children with NPC often have low platelet counts, which might have contributed to the bleeding. Cassi also took drugs that children in the NIH trial didn't. A combination of drugs could have made her more vulnerable.

This was the kind of medical emergency that had worried scientists about uncontrolled experiments. Dr. Porter reached Caroline Hastings, the girls' doctor, to find out what happened. Even though Cassi wasn't in the NIH trial, he was obligated to report anything about the drug's risks to an NIH review board and to the FDA.

Dr. Porter's drug trial had also run into trouble. Patient No. 1, a 13-year-old girl, developed an infection. Bacteria normally found on the skin and scalp had grown in the surgically implanted catheter. After two weeks of antibiotics, the bacteria remained. The catheter had to go.

Then the catheter in patient No. 3 showed signs of infection. Tests later found no infection, but the family, after consulting with doctors, had it removed.

Dillon became the only patient left in the NIH trial.

A few days after Cassi fell ill, the Papiers hosted a charity baseball game featuring the Bowie Baysox, a minor-league team of the Baltimore Orioles. "Dillon was on,'' his mother, Darrile Papier, said. The boy threw out the first pitch and headed to the dugout to talk to his favorite players. He hugged friends in the stands.

After the game, the family spent the night at the Children's Inn at the NIH. The next morning, April 15, Dillon received his third infusion of cyclodextrin and then took a nap.

When he woke up, he didn't feel well. He vomited. His fever spiked. Additional samples of his blood and spinal fluid were examined for infection. Doctors were alarmed. They showed the results to the Papiers. "The numbers were crazy,'' Ms. Papier said.

Doctors worried that Dillon's fever and vomiting signaled bacteria had spread from the catheter to the brain.

Ms. Papier badly wanted Dillon to continue receiving the drug. Since the trial started, she said, Dillon's walk was more steady. The boy seemed better able to understand and was more articulate.

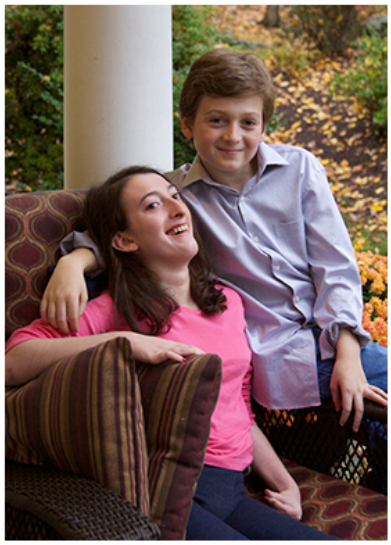
But the doctors didn't want to risk a brain infection. The catheter had to come out right away. The Papiers agreed.

An operating room was prepared. At 11:30 p.m., nurses wheeled Dillon into surgery.

Dr. Porter understood the trial required difficult choices—which children to enroll, as well as who might be disqualified because of declining health.

He knew all the NPC children in his study and their parents. In many families, he also knew siblings and grandparents. Every drug trial requires tough decisions. But with rare diseases, he said, the consequences aren't theoretical: "You know the faces that attach to those consequences."

The Marella family of Greenwich, Conn., had for a year debated whether to seek special permission from the FDA to administer cyclodextrin to their children—as the Hempels had—or wait for a spot in the NIH trial.
Their 13-year-old son Andrew was a good trial candidate, but their 19-year-old daughter Dana was too sick to enroll. She had respiratory infections and other health troubles that landed her in the hospital. She needed a ventilator.



Dana, age 17 and her brother Andrew, age 11 on the Marella's front porch in 2010.

Andrew's symptoms were growing more noticeable. His speech was getting tougher to understand and his gait was awkward. But he looked forward to attending Greenwich High School in the fall with his brother Philip.

Mr. Marella understood that if families didn't enroll in the drug trial, cyclodextrin might never get approved by the FDA. But it was difficult to wait. "As long as things seemed to be moving along at a pace where we weren't sacrificing Andrew's health, that was OK,'' he said.

When the family learned that Andrew was accepted into the trial and would start cyclodextrin in July this year, Mr. Marella made plans for the trip to the NIH.

But the day after Dillon got sick, Dr. Porter told the NIH review board he was suspending the trial.

In a conference call with parents, Dr. Porter said he would ask the FDA for permission to restart the trial but they would have to administer cyclodextrin in a different way. Dr. Porter hoped the trial could resume in the fall.

Mr. Marella was dejected. Andrew had been next in line.

In June, the Marellas held their annual benefit. The Beach Boys played and the event raised more than $400,000. Soon after, Dana got sick again.

At the hospital, doctors found her kidneys weren't functioning properly. They made plans for dialysis. On July 9, tests showed Dana's liver had stopped working. Three days later, she died.

The funeral Mass was at St. Catherine of Sienna Church in Riverside, Conn., a few miles from the Marellas' home. One speaker, the Rev. Drew Williams, recalled how Dana sang Broadway songs at the top of her lungs, and that she still went to summer camp after she couldn't walk.

The Rev. Mr. Williams, of the Trinity Church in Greenwich, singled out the work of scientists and families to find a treatment. As a community, he said, "We have to be honest and say that this is not the ending that we hoped for."

Parents of children with NPC joined the long line of mourners for a turn to console Dana's mother, Andrea. "All these parents, we knew each other,'' Mrs. Marella said. "And one by one, we lost our children.''

Dana's death made the Marellas reconsider their decision to wait for the NIH trial. They wanted Andrew on cyclodextrin right away.

In late August, while Andrew was at his first day of high school, Mr. Marella said, “This is a rough awakening for all of us. We know it’s a fatal disease. We tell people it’s a fatal disease, but there was faith it wouldn’t affect this family.’’

Shortly after Dana’s funeral, Andrew started having seizures. “To lose your child and then 11 days later have this happen?’’ Mrs. Marella said. “We have strong faith, but even we said, ‘Enough.’ ’’

The neurologist said he wasn’t sure if the seizures were caused by the progression of NPC disease or if they were a reaction to Dana’s death. A family friend was at the Marella house when Andrew had a seizure. Afterward, the boy asked her, “Am I going to die from this?’’

Andrew hadn’t yet asked his parents that question. “We always maintain that he will be fine,’’ Mr. Marella said. When they discuss NPC with Andrew, now 14, they tell him the Zavesca is helping and more drugs are on the way. Since Dana’s death, Mr. Marella worries the assurances ring hollow.

A few weeks after Dana’s funeral, Mr. Marella went to Baltimore to attend the annual meeting of the National Niemann-Pick Disease Foundation.

A small memorial was set up at the front of the hotel conference room. Photos of Dana and others who died in the past year rested on tables that lined the way to the podium. Candles illuminated each child’s face. “It’s not just about science,’’ Mr. Marella said of the memorial. “It’s about life.’’

After the morning presentations, Mr. Marella ate lunch and left. There were still two more days in the conference, but Mr. Marella headed home.

Even with the prospect of the trial restarting, Mrs. Marella didn’t want to wait any longer for Andrew. “Why are other families getting their kids on cyclodextrin, and why are we sitting back and letting the disease take hold?’’ she asked. “We’ve waited and waited. We’ve lost one. All the more reason to hurry it up.”

Mr. Marella took steps to apply for FDA permission to get Andrew on cyclodextrin. He didn’t withdraw his son from the trial. He said he would follow whichever route was the shortest.

Mr. Marella had already set up a college fund for Andrew and planned to use it. “I just assume we’re going to get there,’’ he said.

Mrs. Marella doesn’t look that far ahead.

“I take each day,’’ she said.

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