An 8-year-old girl with leukemia receives an experimental cell therapy.

PHOTO: BILL O'LEARY/*THE WASHINGTON POST* VIA GETTY IMAGES

DRUG DEVELOPMENT

Children with cancer get more access to experimental drugs

New U.S. law will require pediatric cancer clinic trials

By **Charles Schmidt**

Jacob Goodman was only 8 years old when he was diagnosed with medulloblastoma, the most common pediatric brain cancer. A music fan who played the piano and sang in his older brother's rock band, he was treated with surgery, radiation, and chemotherapy. But like other children with cancer, he was denied access to clinical trials underway in adults for newer, molecularly targeted treatments, and he died within 2 years. "My son was given 40-year-old drugs," says Jacob's mother Nancy, who lives in Washington, D.C. "They did not work."

Better access for children to experimental cancer drugs could be around the corner, thanks in large part to the efforts of Jacob's mom. On 3 August, the U.S. Senate followed the lead of the House of Representatives and passed the Research to Accelerate Cures and Equity for Children (RACE) Act, which will close loopholes in U.S. drug approval guidelines that companies have exploited to avoid enrolling children in clinical cancer research. Those firms often fear the risk and financial burden that comes with testing new and potentially dangerous compounds in children with cancer, but the scientific rationale for moving ahead with such trials "has never been greater," says Charles Mullighan, co-leader of the Hematological Malignancies Program at St. Jude Children's Research Hospital in Memphis, Tennessee. "We just can't wait anymore for approvals in other indications while pediatrics takes a back seat," he says.

Cancer kills more U.S. children than any single disease, but it's still relatively rare in kids—finding enough kids for trials is another reason why firms lean toward testing new anticancer compounds in adults. The result is that children get the drugs only after they've been approved for adults, which can take a decade or more. In most pediatric cancer trials today, investigators simply tweak doses for already approved agents.

Congress initially tried to improve children's access to clinical trials in 2003, when it passed the Pediatric Research Equity Act (PREA). The law required drug companies to test experimental drugs being developed for adults in children as well. But it waived that demand for nonpediatric conditions, such as Alzheimer's. Adult cancers often occur in different organs, and have different causes, than pediatric malignancies, so the PREA also exempted cancer drugs.

But advances in genetics have shown that childhood and adult cancers affecting different organs can share molecular defects. Mutations affecting the gene for an enzyme called ALK, for instance, are found in adult lung cancer as well as in pediatric blood and brain cancers, and all might respond to ALK inhibitors. The RACE Act directs companies to follow the PREA's demands when a drug's target is common to pediatric and adult malignancies. The law also provides that experimental drugs be made available to children with rare "orphan" cancers.

Goodman herself drafted the language of the RACE Act after her son's death, and circulated it to officials with the Food and Drug Administration (FDA) and other parties. She also formed an advocacy group, Kids v Cancer, and spent years gathering endorsements from hundreds of organizations, cancer centers, and children's hospitals. The RACE Act ultimately won bipartisan support, and was shuttled through the Senate by Marco Rubio (R–FL) and Michael Bennet (D–CO). President Donald Trump is expected to approve it. The law will take effect in 3 years, Goodman says, after FDA holds public hearings and drafts a guidance document describing the specific scenarios that trigger the PREA's testing requirements.

"It will be up to the companies to develop their approaches on a case-by-case basis," Goodman says. "In some cases, it could make sense for them to run a separate clinical trial with a pediatric cohort, and in others to add a pediatric arm to an adult study." She adds that FDA will maintain lists of molecular targets that are exempted from the PREA's requirements because they don't occur in pediatric cancers, as well as a list of targets that don't get such waivers.

Kathleen Neville, a pediatric hematologist-oncologist in Little Rock and immediate past chair of the American Academy of Pediatrics's Committee on Drugs, says that on balance, the RACE Act is a positive step toward making more cancer treatments available in pediatric settings. "But we don't want to wind up with unintended consequences from studying these agents in children too soon," she cautions. "Molecularly targeted drugs are fairly new."

Neville and others also note that the RACE Act raises logistical questions about how pediatric trials with experimental cancer drugs can be performed cost-effectively. Adding trials with children to clinical research amounts to a "huge extra burden shouldered by an industry that answers to shareholders," Neville says. "The potential risk is that companies will simply pass on the costs in the form of higher drug prices. … We're just going to see how this all unfolds." ■

Charles Schmidt is a journalist in Portland, Maine.