Rare Pediatric Cancer Successfully Treated with New Targeted Therapy

Infant's tumor regression shows promise for experimental treatment



When a baby's life was threatened by a rare pediatric cancer that would not respond to surgery or chemotherapy, doctors at Nemours Children's Hospital rapidly, successfully shrank the tumor by 90 percent using an experimental treatment, according to a new study published online in Pediatric Blood and Cancer. The now-20-month-old girl achieved the remarkable improvement by receiving a drug called LOXO-101 that was being tested on adults, researchers reported.

"Most infants and children with infantile fibrosarcoma (IFS) can be cured through surgery and chemotherapy. When our patient's disease progressed in spite of these treatments, we had to investigate new options that could target the disease," said Dr. Ramamoorthy Nagasubramanian M.D., lead author of the manuscript, division chief of pediatric hematology-oncology at Nemours Children's Hospital. "The dramatic reduction in tumor size shows early but promising evidence of the potential for LOXO-101 to provide significant benefit for pediatric patients with NTRK gene fusions."

Nemours' oncology team operated on the girl at 6 months to remove a large tumor located in the neck and face. The tumor did not respond to standard chemotherapy and relapsed after extensive surgery. Genetic testing confirmed an ETV6-NTRK3 gene fusion, which is frequently found in IFS. At the time, LOXO-101 was in a Phase 1 multi-center basket trial in adults. Working with Nemours, Loxo Oncology, Inc., a biopharmaceutical company developing highly selective medicines for patients with genetically defined cancers, was able to expand the trial to children and enroll her.

An special liquid formulation of LOXO-101 was developed, with a pharmacokinetic approach that weighed all the variables, to determine the proper size dosage for each case. Response to the drug was assessed by MRI imaging every 4-8weeks.

"Although some genetic drivers of cancer are found in both pediatric and adult patients, there are few targeted therapies available to children with cancer," said Josh Bilenker, M.D., chief executive officer of Loxo Oncology. "We've known that NTRK fusions play an important role in many pediatric cancers, and this case study is a first step in demonstrating that a selective TRK inhibitor can provide benefit to these children. We are dedicated to the rapid development of LOXO-101 in pediatric cancer patients."

At the time of this manuscript, the patient is in the fifthcycle of LOXO-101, with good response confirmed using Response Evaluation Criteria in Solid Tumors (RECIST), and is achieving normal developmental milestones. The patient has experienced no adverse events related to LOXO-101.

"The development of these inhibitors for pediatric patients has likely lagged behind adult development because of the limited availability of comprehensive genomic profiling of rare pediatric tumors, and the generally favorable outcomes of using conventional treatments," said Dr. Ramamoorthy Nagasubramanian. "However, this case underscores the promise and life-saving potential of targeted therapies for children."

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