Drug Successfully Targets Cancers with Tumor-Specific Gene Mutations

Pediatric and adult cancers with one of three fusion genes responds well to a new drug, larotrectinib, according to a study published today in the *New England Journal of Medicine.* The drug is designed to target a specific tumor gene mutation known as tropomyosin receptor kinases (TRK) that can occur in various tumor types.

“This drug represents a changing paradigm in cancer care where we evaluate a tumor, not only by where it exists in the body, but by the genetic mutations that are driving its growth,” said Ramamoorthy Nagasubramanian, MD, an author of the study and division chief of pediatric hematology-oncology at Nemours Children's Hospital.

The study integrates findings of three phases of research, including an adult phase 1, a pediatric phase 1/2, and an adolescent/adult phase 2 study, to report on the safety and efficacy of the drug. Fifty-five patients with TRK fusion-positive cancers, detected by molecular profiling as routinely performed by each site, were enrolled across the study sites. Patients ranged in age from 4 months to 76 years old and had 17 unique cancer diagnoses, including infantile fibrosarcoma, salivary gland tumors, and thyroid cancer. Each patient received two daily doses of the drug in pill or liquid form.

Overall 75 percent of patients had their tumors respond to the treatment, with 13 percent achieving a complete response and 62 percent achieving a partial response. Responding patients remained on treatment or underwent surgery with curative intent. The median time to response was 1.8 months (range 0.9 to 6.4). The median duration of response and progression-free survival had not been reached, but after one year, 71 percent of patients with a response were ongoing and 55 percent of all patients remained progression-free. The treatment was well-tolerated by patients. Clinically significant adverse events were uncommon and most frequently included inflammation in the liver and other organs (alanine or aspartate aminotransferase increase), fatigue, vomiting, and dizziness.

“This study’s design, simultaneously testing the efficacy and safety in adults and children, represents a strong model to follow to help advance pediatric cancer research,” said Nagasubramanian. “In an era where we are not only treating tumors by names, but by their genetic signature, this research allows us to move the field forward without leaving children behind, as is so often the case in pediatric research.”

The study authors note that additional data reflecting longer follow-up and a larger patient population will provide further insight into the safety profile of the drug, as well as the durability of the response.

Drilon, A, et al. "Efficacy of Larotrectinib in TRK Fusion-Positive Adult and Pediatric Cancers."*New England Journal of Medicine* (2018): 22 Feb. 2018. Web.

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