First targeted therapy for children with achondroplasia shows persistent height gain

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Children with achondroplasia, the most common form of disproportionate short stature, grow taller with trends in improved body proportions after two years of daily vosoritide treatment, a new study analysis finds. Results of the industry-sponsored study will be presented at ENDO 2021, the Endocrine Society's annual meeting.

"This is the first robust evidence of a precision therapy for achondroplasia," said the lead investigator, Ravi Savarirayan, M.D., Ph.D., a professor at Murdoch Children's Research Institute at Royal Children's Hospital in Parkville, Australia.

Achondroplasia is a genetic bone growth disorder whose characteristics include short arms and legs and an adult height typically below 4 feet, 6 inches. Medical complications of achondroplasia include spinal stenosis (narrowing of the spinal column) and spinal cord compression, bowed legs, permanently swayed lower back and sleep apnea. Treatment focuses on relieving symptoms and is often surgical. There is currently no effective treatment to increase height in these patients.

Vosoritide is an investigational drug targeting the overactive signal in the growth plate that prevents bone growth in children with achondroplasia, Savarirayan said. The goal of treatment, he added, is better medical, functional and psychosocial outcomes.

"We hope that improved height and body proportion will increase independence and alleviate some of the long-term issues, such as spinal

stenosis," Savarirayan said.

A prior study in children ages 5 to 17 with achondroplasia showed that one year of daily injections of vosoritide significantly improved the participants' annualized growth velocity (AGV), which is the annual height gain, compared with a placebo, or dummy drug. The new study extends the data analysis after an additional year of continuous vosoritide treatment.

In the extension study, 61 children who had received the placebo the first year switched to vosoritide therapy, and 58 children continued vosoritide treatment for another 52 weeks. Final follow-up data were available for 108 of the 119 children.

Children who received two years' vosoritide therapy had a baseline mean AGV of 4.28 cm/year. After one year of treatment, mean AGV was 5.71 cm/year and after the second year mean AGV was 5.65 cm/year. After the second year of treatment, they also had a better height z-score, which is a measure of height relative to that of a similar population of average height.

Additionally, the children showed trends towards a better ratio of upper to lower body segments. Savarirayan said an improved body proportion often means the children can now more easily reach objects and perform self-care, such as toileting. Longer term follow-up is ongoing where additional data on quality of life, functional measures and final adult height will help to confirm the clinical relevance of these improvements in growth and proportionality.

These findings, Savarirayan said, indicate that vosoritide has persistent two-year beneficial effects on growth in children with achondroplasia.

Furthermore, the data showed that in children who received one year of

vosoritide therapy after stopping placebo, growth also improved.

Vosoritide is under study in children whose growth plates are still open. They can receive the drug until they are near final adult height, which is 16 to 18 years old, according to Savarirayan. While these data are encouraging at showing a durable treatment effect up to 2 years, the long-term clinical benefits of vosoritide will likely require many more years of evaluation, and we will continue to investigate these important questions as part of the long-term follow-up portion of this study, he said.

Achondroplasia occurs in one in every 15,000 to 35,000 births, according to the National Organization for Rare Disorders.

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