Novel Tx Spurs Growth in Short Stature Kids

BY MIRIAM E. TUCKER

NEW YORK — An investigational combination of recombinant human growth hormone and recombinant human insulin-like growth factor-1 produced significant increases in height velocity and favorable changes in height relative to bone age, according to preliminary study data.

The findings are from an early assessment from an ongoing, 3-year study of prepubertal children with short stature associated with low insulin-like growth factor-1 (IGF-1). The data were presented at the 8th Joint Meeting of the Lawson Wilkins Pediatric Endocrine Society and European Society for Pediatric Endocrinology.

The research was funded by Tercica, Inc., a subsidiary of the Ipsen Group, which developed the human growth hormone and recombinant human insulin-like growth factor-1 (rhGH/rhIGF-1) combination, according to Dr. George M. Bright, Tercica's vice president and medical director, endocrinology.

A total of 106 children have been randomized thus far to one of four arms: 45 mcg/kg of rhGH alone given subcutaneously, or in combination with 50, 100, or 150 mcg/kg of rhIGF-1 (given as a separate injection). The children were all treatment-naive, with otherwise unexplained short stature (height standard deviation score of –2 or less), an IGF-1 SD score of –1 or less and a maximum stimulated GH level of 10 ng/mL or greater. All were prepubertal at the start of the study.

Safety data were available for all 106 children and efficacy data for 36 who completed the first year of the study. For the primary end point, first-year height velocity, the mean values were 9.2 cm/year for the rhGH monotherapy group (n=11), and 10.4, 10.7, and 12.1 cm/year, respectively, for the combinations of rhGH plus 50 (n=7), 100 (n=9), and 150 (n=9) mcg/kg of rhIGF-1.

First-year increases in height SD scores were 0.72, 0.88, 0.91, and 1.1, respectively, Dr. Bright reported at the meeting.

Most of the children appeared to show greater change in height age than in bone age, in this early assessment from an ongoing, 3-year study of prepubertal children with short stature.

The study protocol specified reducing the rhIGF-1 dose if a subject had an IGF-1 score measurement above plus-4. This occurred in seven subjects, three from the 100-mcg/kg rhIGF-1 dose group and four from the 150 mcg/kg dose group. It's not clear that this level actually poses a danger, but it was done as a safeguard, he noted. Most of the children appeared to show greater change in height age than in bone age, he added.

Four serious adverse events have occurred thus far in 2 of the 106 children. A 10-year-old male experienced thrombocytopenia, hematuria, and viral infection and was diagnosed with Evans syndrome. This was considered not drug related, but he did discontinue the study. An 11-year-old male in the 150-mcg/kg rhIGF-1 group had transient papilledema with probable intracranial hypertension, which was considered probably drug related. Treatment was stopped and restarted without recurrence.

Five patients withdrew early from the study, four of them due to adverse events. In addition to the Evans syndrome patient, two had generalized urticaria that was considered drug-related. One had alopecia that was considered possibly/probably drug-related. The fifth withdrew due to noncompliance.

Headache was reported by a fourth of the rhGH monotherapy group and by half of the highest dose combo group, with the two middle groups falling in between. Vomiting occurred in 12%-15% of all four groups. However, only eight patients reported both headache and vomiting. Two children are thought to have had intracranial hypertension, Dr. Bright said.

Transient elevations in transaminases were seen during weeks 0-13 in some of the patients, he said but most were less than 2.5 times the upper limit of normal, and resolved by 13 weeks. ■