Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo-controlled, multicentre trial.

Savarirayan R, Tofts L, Irving Met al. Lancet. 2020 Sep 5;396(10252):684-692 doi: 10.1016/S0140-6736(20)31541-5

Background: Currently there are no effective therapies for achondroplasia. In a previous open-label, phase II study, administration of the recombinant form of C type natriuretic peptide, vosoritide, resulted in sustained increases in growth velocity.

Methods: 1 year, randomised, double-blind, phase 3, placebo-controlled, multicentre trial. 121 children, aged 5 to less than 18 years, 24 sites in seven countries were enrolled.

- Compared once-daily subcutaneous administration of vosoritide with placebo.
- Primary endpoint was change from baseline in mean annualised growth velocity at 52 weeks in treated patients as compared with controls.

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet

Vosoritide Increases Growth in Achondroplasia

Results:

- Change in annualised growth velocity from baseline was +1.71cm/year compared with +0.13 cm/year with placebo (P<0.0001)
- Change from baseline in height Z-score was +0.27 with vosoritide compared with -0.01 with placebo (P<0.0001)
- Adjusted mean difference in annualised growth velocity was 1.57 cm/year in favour of vosoritide (95% CI [1.22-1.93])

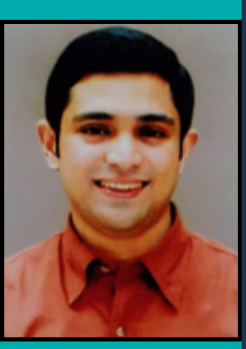
Clinical outcomes:

- Upper to lower body segment ratio did not differ between groups
- Bone mineralization and bone age did not differ between groups
- Adverse events were mild and most frequently reactions to injection sites
- Although 42% developed antidrug antibodies, no neutralizing antibodies were found
- Quality of life was not different with vosoritide

Conclusion: Daily subcutaneous administration of 15 mcg/kg vosoritide in children with achondroplasia resulted in highly significant improvements in annualised growth velocity and height Z-score compared with placebo after 52 weeks.

Key message: This study provides the first, robust evidence for an effective, precision therapy for achondroplasia, underpinning a fundamental change in the clinical management policies, natural growth history and treatment recommendations for children affected by this condition.

EXPERT COMMENT



"Vosoritide, a C-type Natriuretic Peptide, can safely restore endochondrial ossification in children with achondroplasia. However, there is still no data on long-term efficacy of this drug, about its side effects, about how it affects body segment proportionality and whether the final adult height will be increased. Currently listed as an orphan drug by the FDA, the results of the latest trial on vosoritide are promising."

Dr Abraham Paulose, MD, MRCPCH, Post Doctoral Fellow
Paediatric and Adolescent Endocrinologist,
Associate Professor, Department of Pediatrics,
MOSC MCH, Kolenchery, Kerala, India.

DR MANINDER S DHALIWAL
Editor – Academic Pearls
pedpearls@gmail.com

Reference

Savarirayan R, Tofts L, Irving M, Wilcox W et al. Once-daily, subcutaneous vosoritide therapy in children with achondroplasia: a randomised, double-blind, phase 3, placebo-controlled, multicentre trial. Lancet. 2020 Sep 5;396(10252):684-692. doi: 10.1016/S0140-6736(20)31541-5. Erratum in: Lancet. 2020 Oct 10;396(10257):1070.