Vosoritide improves tibial bowing in infants and toddlers with achondroplasia

Poster #42

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Introduction

- Vosoritide, an analogue of C-type natriuretic peptide, is approved for use in children with achondroplasia (ACH)[1]
- By stimulating endochondral bone growth, vosoritide positively impacts body proportionality and quality of life[2,3]
- Tibial bowing is a common orthopaedic complication of ACH, with an incidence of 40%–70%.[4] Tibial bowing is a cause of pain and impaired function for children with ACH and a common reason for surgical intervention, with ~25% requiring surgery[5]
- Here, we assess the impact of vosoritide treatment on the degree of bowing present in the study population

Objective

- To assess the impact of vosoritide treatment on tibial bowing in children with ACH who began treatment aged <5 years

Study design

Following an observational period, children (n = 75) were enrolled and **randomized 1:1** (except for 11 sentinel participants who were assigned to vosoritide) to receive vosoritide or placebo for 1 year

Study 111-206 (NCT03583697)
Randomized, double-blind, placebo-controlled phase 2 trial in children aged <5 years with ACH

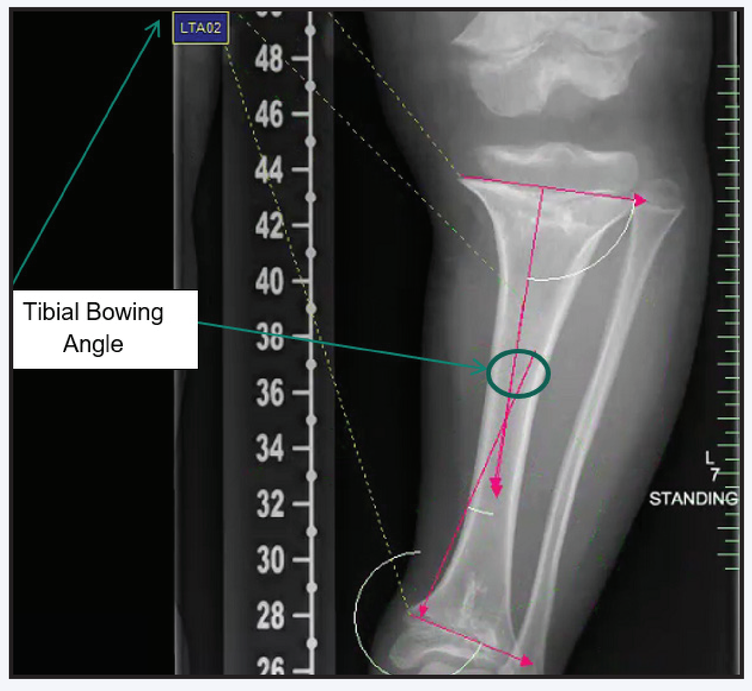
Study 111-208 (NCT03989947)
Ongoing open-label extension study, with participants receiving placebo transitioning to vosoritide

Data shown are based on 3-year observation.
[a]Participants received 30 µg/kg of vosoritide until 2 years of age, then switched to a dose of 15 µg/kg. Vosoritide was administered as a single daily subcutaneous injection.
ACH, achondroplasia.

Tibial bowing analysis

- Image acquisition was standardized across the sites, and X-rays were centrally read by independent radiologists to minimize variability in measurement
- X-rays were taken at baseline and week 52 for the 111-206 study and every 2 years for the 111-208 study
- Degree of tibial bowing was observed radiographically as the linear intersections derived from the upper and lower physeal plates and the mid-shaft of the tibia
- Magnitude of change in tibial bowing was quantified as least squares mean change from baseline, applying an analysis of covariance model, and reported in degrees

Tibial bowing in the left leg



Results

Participants

- The 111-206 total population included 11 sentinel participants who received vosoritide and 64 participants randomized 1:1 to vosoritide or placebo (**Table 1**)
  - The 73 participants who completed 111-206 enrolled in 111-208, the open-label long-term extension
- For the overall 111-206 population, tibial bowing was present in both the left and right legs at baseline

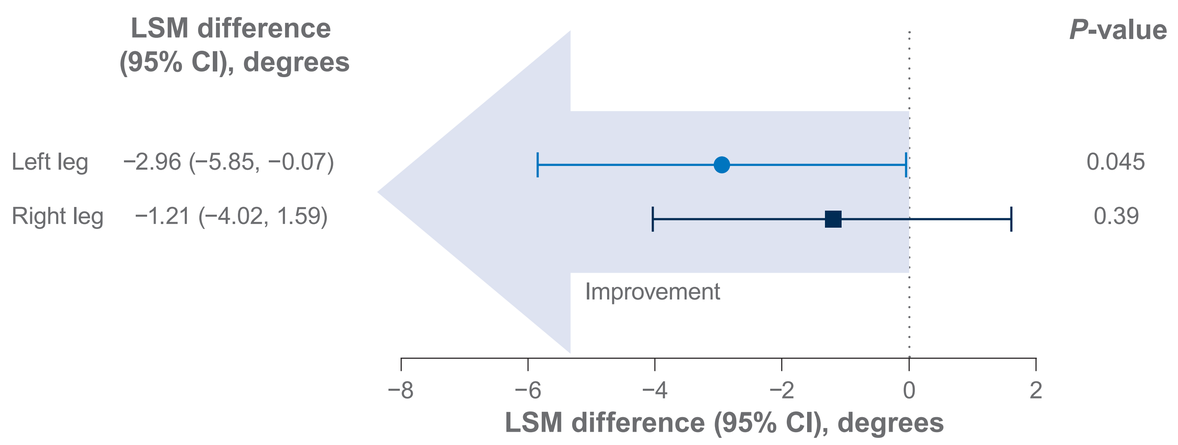
Table 1. Baseline characteristics and growth parameters of all vosoritide-treated participants and those randomly assigned to placebo from 111-206[6]

Characteristic	Total population	
	Vosoritide (n = 43)	Placebo (n = 32)
Age on day 1,[a] months	24.47 (17.66)	27.82 (19.25)
Sex		
Male	25 (58.1%)	13 (40.6%)
Female	18 (41.9%)	19 (59.4%)
Race		
White	29 (67.4%)	25 (78.1%)
Asian	11 (25.6%)	6 (18.8%)
Other[b]	3 (7.0%)	1 (3.1%)
Hispanic or Latino ethnicity	3 (7.0%)	3 (9.4%)
Height Z score[c]	−3.88 (0.90)	−4.28 (1.48)
Baseline tibial bowing angle, degrees		
Right leg	11.81 (6.49), n = 42	11.41 (7.44), n = 32
Left leg	9.98 (7.14), n = 42	12.59 (7.98), n = 32

Data are mean (SD) or n (%). Percentages may not sum to 100 due to rounding.
[a]Day 1 of treatment. [b]Other includes multiple races and Native Hawaiian or other Pacific Islander. [c]Z scores were derived using age-specific and sex-specific reference data (means and SDs) for average-stature children according to the US Centers for Disease Control and Prevention.[7]
SD, standard deviation.

Tibial bowing results

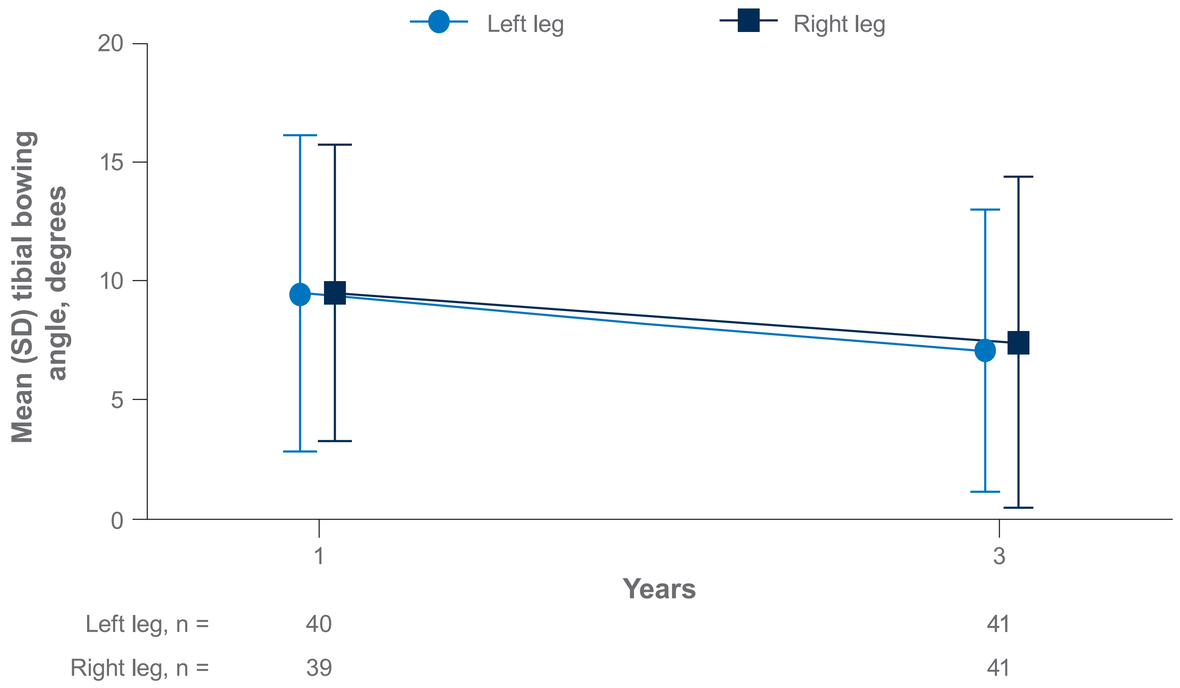
Figure 1. LSM difference between vosoritide and placebo in change from baseline at year 1



CI, confidence interval; LSM, least squares mean.

- After 1 year of treatment, vosoritide improved tibial bowing angle from baseline compared with placebo in both legs (**Figure 1**)

Figure 2. Tibial bowing over time for participants in the 111-206 active arm receiving vosoritide for up to 3 years



Only active participants from the 111-206 study are included because the participants receiving placebo had imaging assessments at different years (ie, years 2 and 4).
SD, standard deviation.

- In 3 years of vosoritide treatment for those who entered study 111-208, tibial bowing angle continued to decrease in both legs (**Figure 2**)

Conclusions

- Treatment with vosoritide significantly improved tibial bowing for children with ACH <5 years old at the start of treatment compared with placebo after 1 year, with continued improvement over 3 years
- These results suggest vosoritide treatment from an early age provides growth increases that positively impact complications of ACH

References

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