Effectiveness of Vosoritide in Children with Achondroplasia Starting Treatment Aged <2 Years: Interim Results from a Japanese Real-World Study

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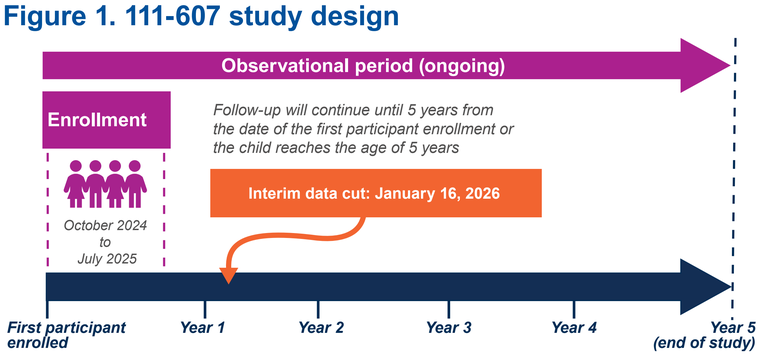
Introduction

- Achondroplasia is a rare skeletal dysplasia caused by impaired endochondral bone growth, disrupting early growth and leading to multisystem complications and surgical interventions[1,2]
  - Foramen magnum stenosis occurs in ~50% of infants and often requires surgical intervention[3]
- Vosoritide, the first approved treatment for achondroplasia, is a recombinant C-type natriuretic peptide analog that stimulates endochondral bone growth[4]
  - Japan was the first country to approve treatment from birth in June 2022[5]
- In the phase 2 CANOPY ACH-2I (111-206) trial, vosoritide safely improved linear growth in children <2 years old at treatment initiation; however, real-world effectiveness data in this population are limited[1]
- Here, we present the first analysis from a real-world study of vosoritide use in Japan among children aged <2 years

Methods

- 111-607 is an ongoing observational study to investigate real-world outcomes in Japanese children with achondroplasia who initiated vosoritide treatment <2 years of age (**Figure 1**)

Figure 1. 111-607 study design



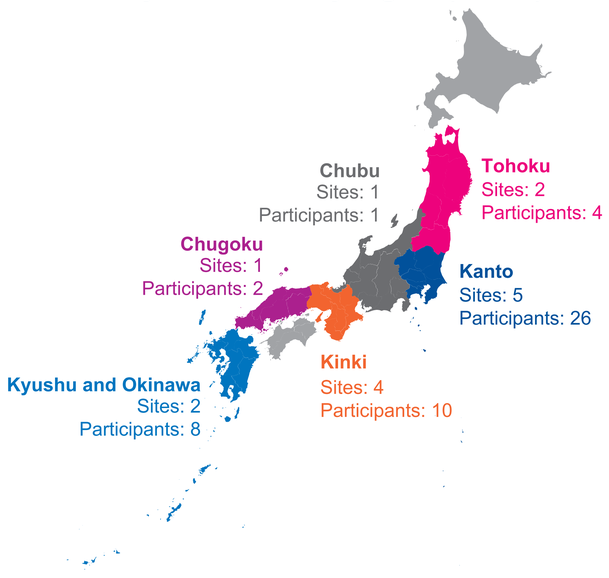
- Participants are monitored at least every 6 months using medical records from routine clinical practice (patients in this young age group typically have medical visits every 1 to 3 months)
  - All participants are also enrolled in an ongoing drug use survey (111-604) required by the Pharmaceutical and Medical Devices Agency to monitor safety
- In this interim analysis, treatment duration, adherence, and changes in height were assessed

Results

Participants and enrollment

- As of July 27, 2025, enrollment was completed with 51 participants
  - Participants were enrolled from 15 different study sites throughout 6 of the 8 regions within Japan (**Figure 2**)
  - The sites with the highest enrollment were The University of Tokyo Hospital and Tokyo Metropolitan Children's Medical Center, Clinical Genetics Department, with each enrolling 7 children

Figure 2. Study enrollment by region (N = 51)



- Three participants were receiving concurrent growth hormone and were excluded from this analysis (**Table 1**)

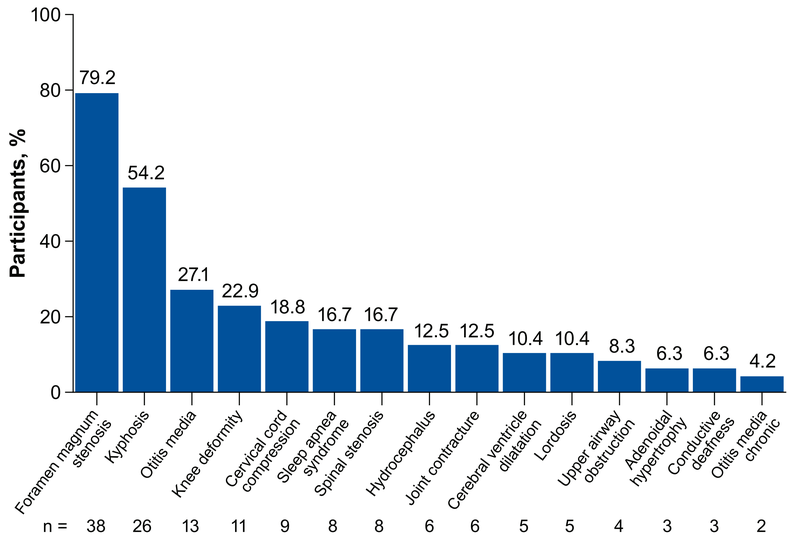
Table 1. Participant baseline characteristics

Characteristic	Overall (N = 48)
Age at enrollment, months, mean ± SD	23.43 ± 12.26
Age at start of treatment, months, mean ± SD (min, max)	8.42 ± 6.26 (1.3, 22.8)
Sex, n (%)	
Male	27 (56.3)
Female	21 (43.8)
Race, n (%)	
Asian, Japanese	46 (95.8)
Asian, other	1 (2.1)
Multiple	1 (2.1)

Excluding 3 participants concurrently receiving growth hormone.
SD, standard deviation.

- At the time of enrollment, 44/48 (91.7%) participants had been diagnosed with any achondroplasia-related medical history condition (**Figure 3**)

Figure 3. Achondroplasia-related medical history diagnoses

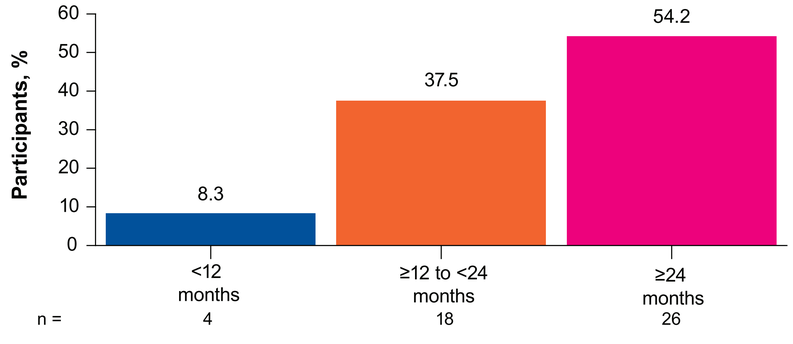


Medical history is shown for >1 participant reporting each diagnosis.

Treatment duration and adherence

- Mean treatment duration in the 48 participants in this analysis was 20.0 (minimum, maximum: 2.9, 32.6) months (**Figure 4**)

Figure 4. Vosoritide treatment duration



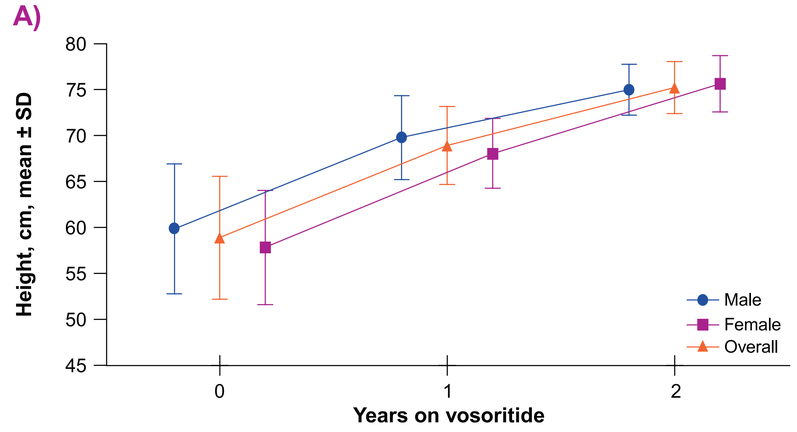
- Treatment adherence was high, with no treatment interruptions (defined as >7 consecutive missed doses) after enrollment

Effectiveness

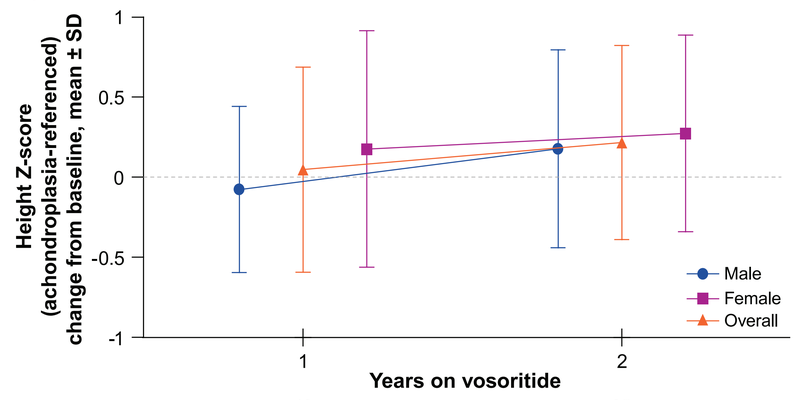
- Height continued to increase over time to a mean (standard deviation [SD]) of 75.0 (2.76) and 75.6 (3.04) cm for male and female participants, respectively, 2 years after treatment initiation (**Figure 5A**)
- Achondroplasia-referenced height Z-score improved from baseline by mean (SD) 0.18 (0.56) after 2 years of treatment for males; for females, improvement occurred after 1 year of treatment and continued through 2 years of treatment for a mean (SD) improvement from baseline of 0.27 (0.61) (**Figure 5B**)

Figure 5. Height (A) and achondroplasia-referenced height Z-scores (B) over time

A)



B)



Height Z-scores were derived using age- and sex-matched reference data from a US achondroplasia natural history cohort (Hoover-Fong et al, 2021 [CLARITY]).[6]
SD, standard deviation.

Conclusions

- In Japan, children with achondroplasia who initiated vosoritide treatment early had high treatment adherence and steady improvements in growth after at least 12 months of treatment, consistent with results seen in clinical trials[1]
- Future reports will highlight descriptive, time-to-event analyses including rates of achondroplasia-related surgeries and changes in brain morphology assessed using magnetic resonance imaging

References

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Disclosures

SM and **HTanaka** have nothing to disclose. **TK** has received honoraria from BioMarin Pharmaceutical Inc. **VH** and **JMP** are employees and stockholders of BioMarin (UK) Ltd. **SR** and **AD** are employees and stockholders of BioMarin Pharmaceutical Inc. **HTokuoka** is an employee and stockholder of BioMarin Pharmaceutical Japan KK. **TM** received lecture fees from Alexion Pharma Japan, BioMarin Pharmaceutical Japan KK, and Kyowa Kirin.

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