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Three-year real-world vosoritide safety and effectiveness in children with achondroplasia in Japan

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JSPE COI Disclosure

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Conflict of Interest Disclosure

Companies with which the presenting author and co-authors have financial relationships relevant to this presentation:

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Disclosure of artificial intelligence (AI) use

- The authors disclose that no AI was used in the preparation of this presentation

Introduction

- Achondroplasia is a skeletal dysplasia caused by pathogenic variants of the *FGFR3* gene that impair endochondral bone growth[1,2]
- Vosoritide is a C-type natriuretic peptide (CNP) analog that stimulates bone growth
  - Clinical trials demonstrated sustained improvements in annualized growth velocity and height Z-score with vosoritide across infants, children, and adolescents with achondroplasia, with a favorable long-term safety profile[3–6]



In June 2022, Japan was the first country to approve vosoritide for use from birth through epiphyseal closure, followed by subsequent approvals in the US and Australia

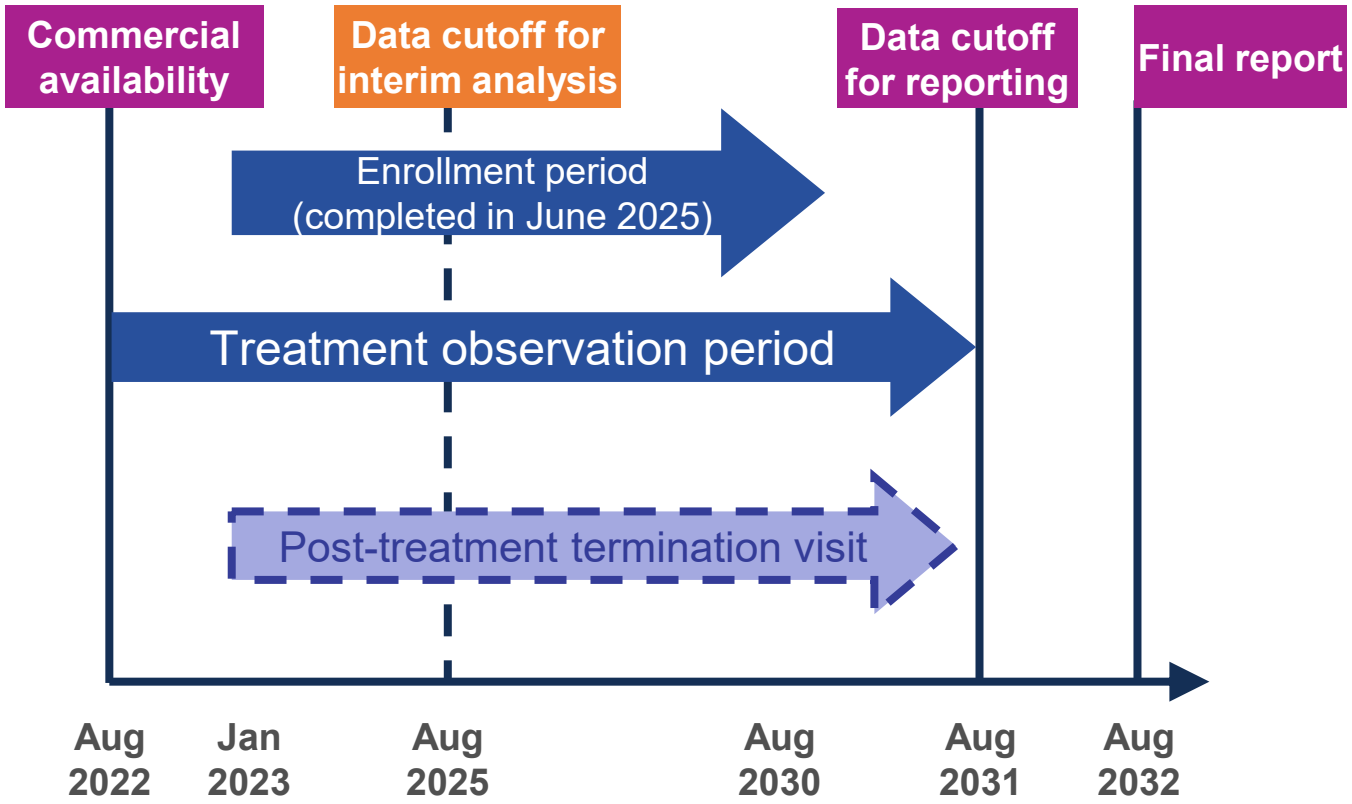
- The ongoing post-marketing safety surveillance study (study 111-604) provides real-world data on the safety and effectiveness of vosoritide in children with achondroplasia in Japan

Objective: To report up to 3 years of real-world safety and effectiveness data from an ongoing drug use survey of vosoritide in children with achondroplasia in Japan

1. Foreman PK, et al. *Am J Med Genet A.* 2020;182(10):2297–316. **2.** Savarirayan R, et al. *Nat Rev Endocrinol.* 2022;18(3):173–89. **3.** Savarirayan R, et al. *N Engl J Med.* 2019;381(1):25–35. **4.** Savarirayan R, et al. *Lancet.* 2020;396(10252):684–92. **5.** Savarirayan R, et al. *Med.* 2025;6(5):100566. **6.** Savarirayan R, et al. *Lancet Child Adolesc Health.* 2024;8(1):40–50.
FGFR3, fibroblast growth factor receptor 3 gene.

Study design

- Study 111-604 is an ongoing post-marketing surveillance study collecting prospective data from the medical records of children and adolescents with achondroplasia who have been prescribed vosoritide in Japan since August 2022
- This interim analysis includes children enrolled in the 111-604 study from January 2023 to June 2025



Adherence

Treatment interruptions
Discontinuations

Safety[a]

Safety events
Safety events of special interest
Adverse drug reactions
Achondroplasia-related surgical events

Efficacy

Annualized growth velocity
Height Z-score (achondroplasia-referenced)[b]

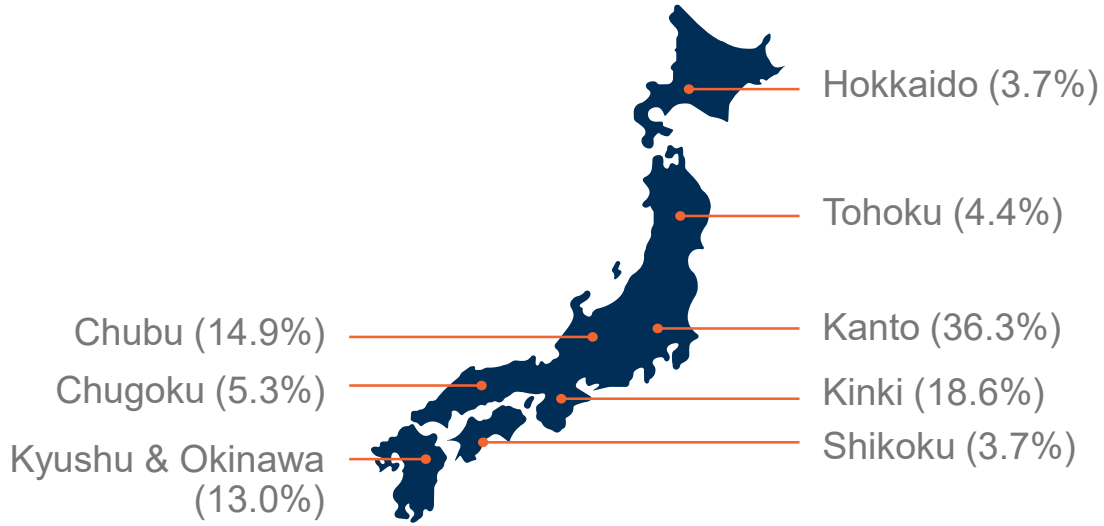
[a]Coded using MedDRA/J version 28.0. [b]Height Z-scores were referenced to age- and sex-matched untreated children with achondroplasia (CLARITY).[1]

1. Hoover-Fong JE, et al. *Orphanet J Rare Dis*. 2021;16(1):522.

MedDRA/J, Japanese translation of Medical Dictionary for Regulatory Activities.

Participant disposition

Study participants were enrolled across all 8 regions of Japan at 160 study sites



At the data cutoff (August 25, 2025), **632** participants were enrolled and **322** consented to publication.
Of these, **118** participants were available for effectiveness analysis at 12 months post treatment initiation in children from birth to ≥11 years of age

Participants enrolled
N = 632

↓

Quality-checked data
Consented to publication
n = 322

↓

Safety analysis
n = 322

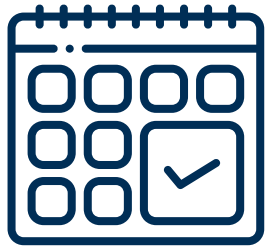
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Effectiveness analysis
(on-treatment 12 months)
n = 118

Baseline characteristics and adherence

	Participants (N = 322)
Sex, n (%)	
Male	168 (52.2)
Female	154 (47.8)
Age at treatment initiation, months, mean ± SD	
Mean ± SD	70.4 ± 51.0
Median (range)	65.0 (0.0–199.0)
Prior growth hormone use, n (%)	14 (6.3)
Growth parameters, mean ± SD	
Body length/standing height, cm	86.7 ± 23.3
Height Z-score (CDC-referenced)	−4.4 ± 1.5
Height Z-score (achondroplasia-referenced)	0.27 ± 1.5
Actual treatment period, months	
Mean ± SD	26.6 ± 8.1
Median (range)	29.3 (0.5–35.7)

- Sixteen participants (5.0%) discontinued vosoritide treatment due to the following:
  - Doctor's judgment (n = 7)
  - Other (n = 7)
  - Safety events (n = 2)
- Six participants (1.9%) had a treatment interruption (missing >7 consecutive days of treatment)



CDC, US Centers for Disease Control and Prevention; SD, standard deviation.

Vosoritide demonstrates a favorable safety profile

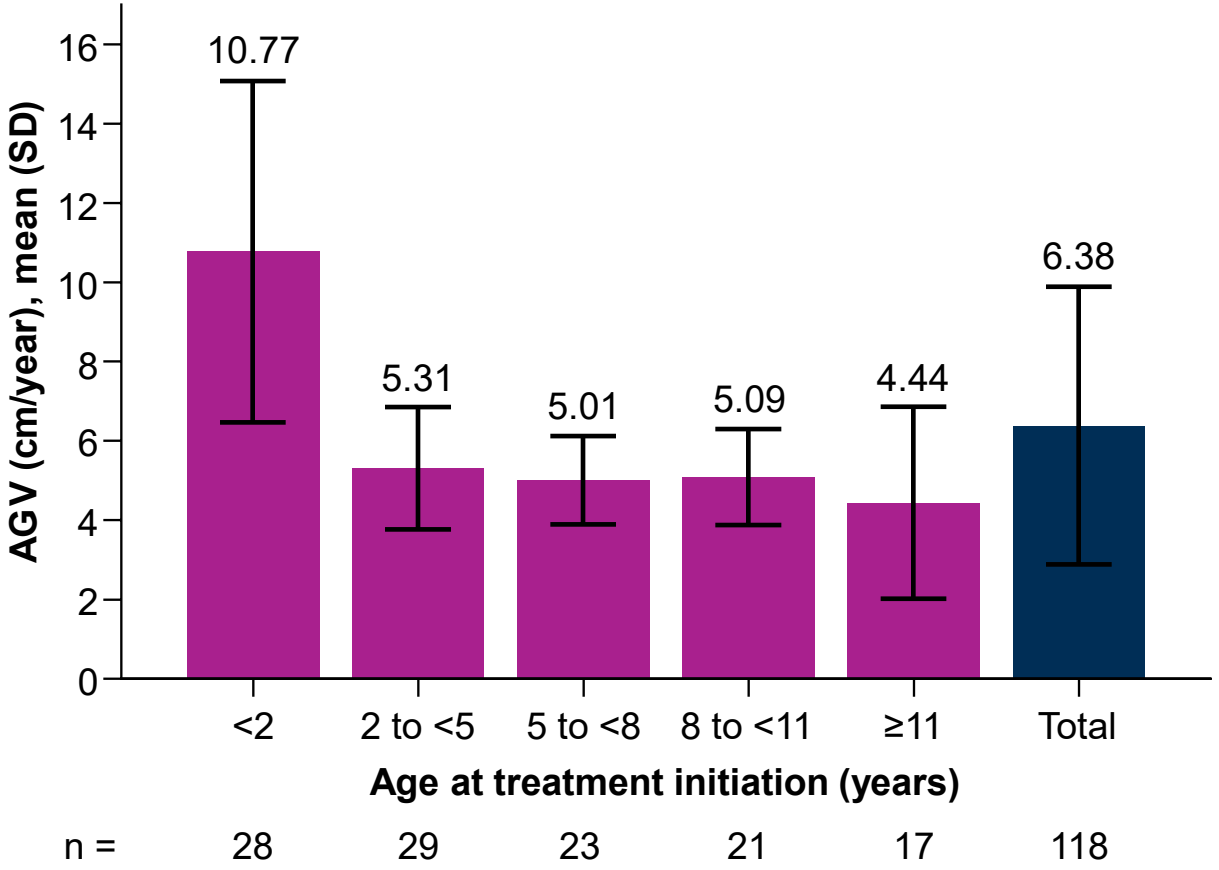
	Participants (N = 322)
Participants with adverse drug reactions, n (%)	15 (4.7%)
Participants with serious adverse drug reactions, n (%)	1 (0.3%)
Foramen magnum stenosis	1 (0.3%)
Participants with achondroplasia-related surgical events (≥2 participants), n (%)	39 (12.11%)
Limb lengthening/elongation	9 (2.8%)
Foramen magnum decompression	7 (2.2%)
Myringotomy tubes	7 (2.2%)
Adenoidectomy	7 (2.2%)
Surgery for limb deformity	3 (0.9%)
Tonsillectomy	2 (0.6%)
Tympanostomy	2 (0.6%)
Surgery for postoperative limb lengthening complications	2 (0.6%)
Other	3 (0.9%)

- No events associated with blood pressure reduction were observed
- Four of 322 (1.2%) participants had bone- or joint-related events
- Serious safety events were reported in 4 of 322 (1.2%) participants
  - Bronchitis (n = 1)
  - RSV infection (n = 1)
  - Abdominal distension (n = 1)
  - Gastroenteritis viral (n = 1)
  - Foramen magnum stenosis (n = 1)



RSV, respiratory syncytial virus.

Annualized growth velocity at **12 months** of follow-up



At 12 months post treatment initiation, mean AGV was

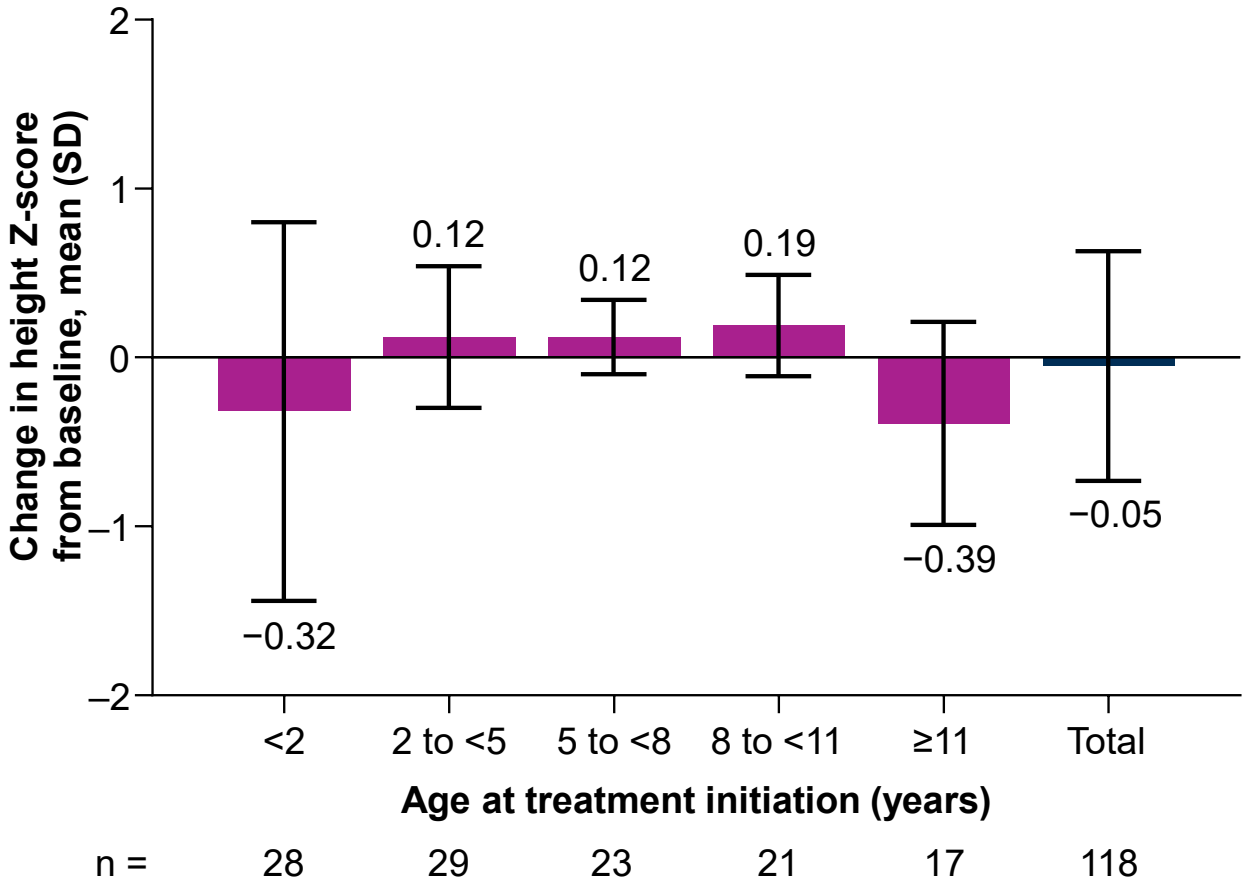
6.38

cm/year overall

and was highest in children who initiated treatment at <2 years of age

AGV, annualized growth velocity; SD, standard deviation.

Change in height Z-scores from treatment initiation after 12 months **(NGS-referenced)**

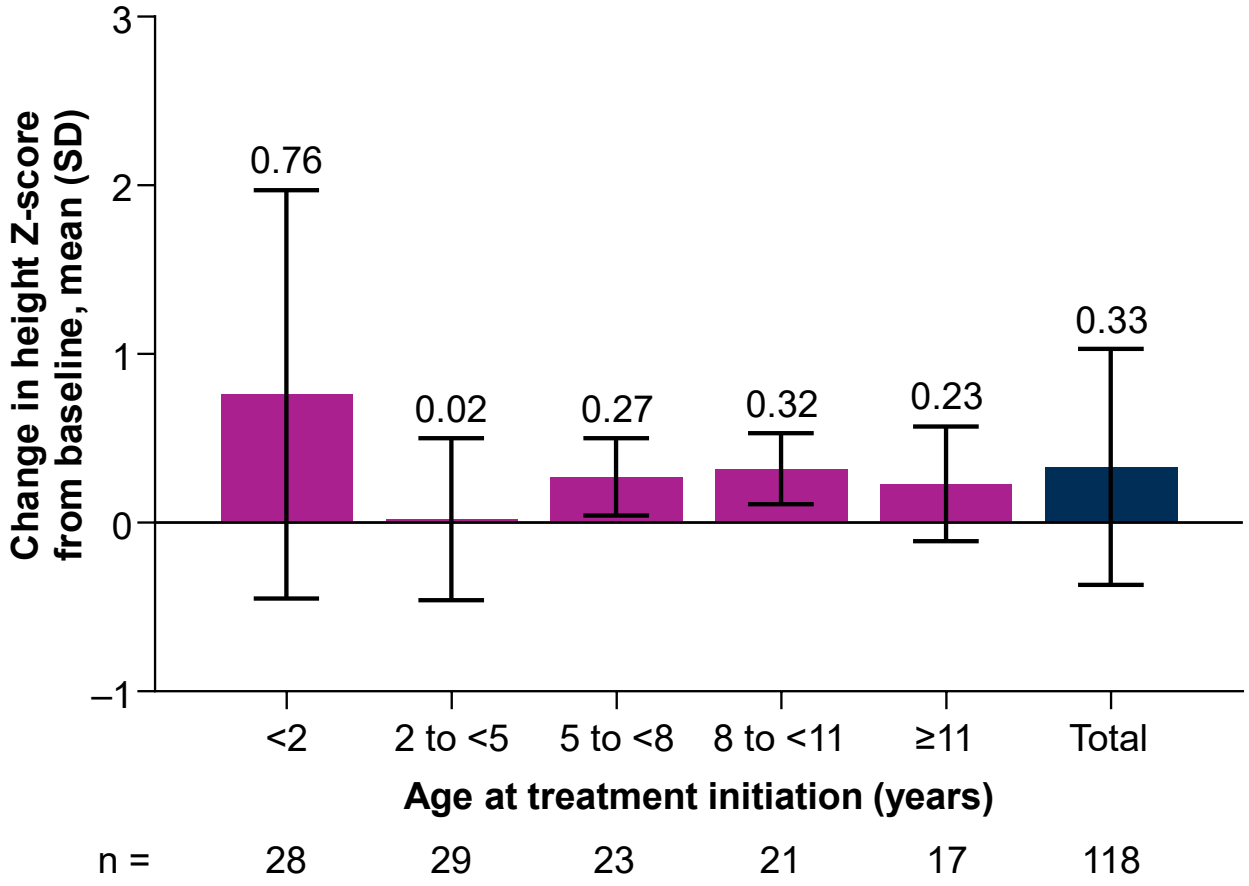


At month 12, mean NGS-referenced height Z-score **numerically increased in children aged 2 to 11 years** at treatment initiation

Change from baseline was **–0.05 overall**

Height Z-scores were referenced to age- and sex-matched Japanese children of average stature (2000 NGS).
NGS, National Growth Survey on Preschool Children & School Health Statistics Research; SD, standard deviation.

Change in height Z-scores from treatment initiation after 12 months **(achondroplasia-referenced)**



Mean achondroplasia-referenced height Z-score had numerical increases from baseline by

0.33 overall,

including increases in children

<2 and ≥11 years of age

at treatment initiation

Height Z-scores were referenced to age- and sex-matched to untreated children with achondroplasia (CLARITY).[1]

1. Hoover-Fong JE, et al. *Orphanet J Rare Dis*. 2021;16(1):522.

SD, standard deviation.

Conclusions



Vosoritide was associated with a favorable and predictable safety profile, with low incidences of adverse drug reactions and serious safety events in Japanese children from birth to ≥11 years of age



Vosoritide treatment was associated with improved growth outcomes across age groups, with the highest AGV and achondroplasia-specific height Z-scores observed in children who initiated treatment before 2 years of age



These interim real-world data support the safety and effectiveness of vosoritide treatment in Japanese children from birth through adolescence

AGV, annualized growth velocity.

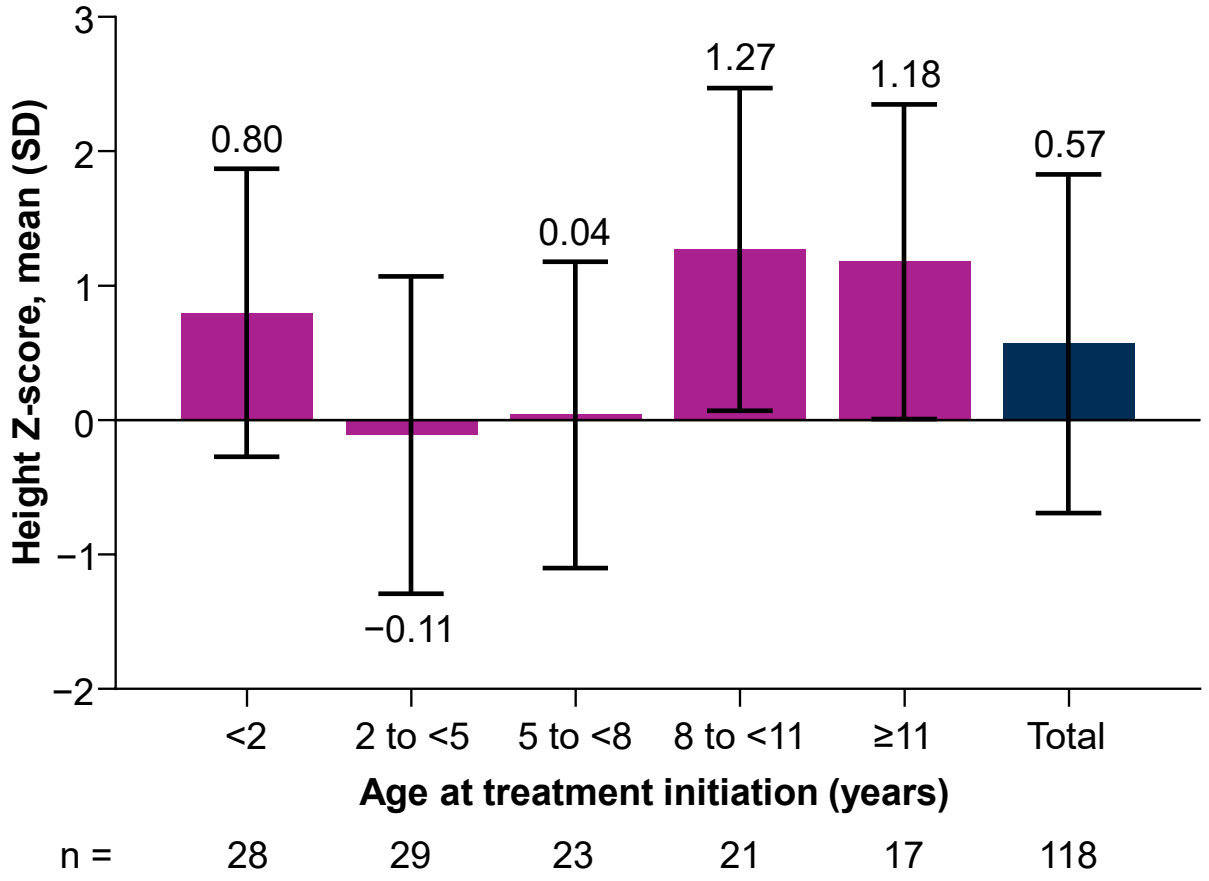
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Height Z-scores at 12 months after treatment initiation **(achondroplasia-referenced)**



Mean achondroplasia-referenced height Z-score was

0.57

overall,

with the highest values observed in children who initiated treatment at 8 to <11 years and ≥11 years of age

Height Z-scores were referenced to age- and sex-matched untreated children with achondroplasia (CLARITY).[1]

1. Hoover-Fong JE, et al. *Orphanet J Rare Dis*. 2021;16(1):522.

SD, standard deviation.