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Vosoritide safety and effectiveness in young children with achondroplasia aged ≤3 years and with up to 36 months of follow-up from the Japanese post-marketing safety surveillance study (111-604)

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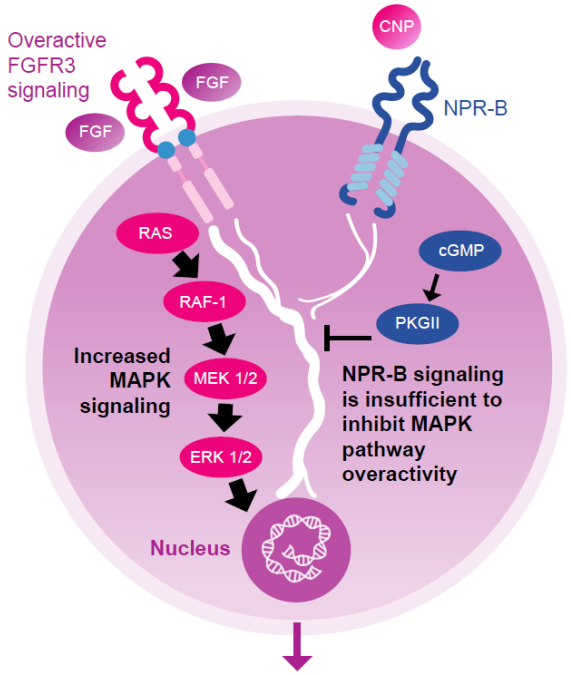
Conflicts of interest

- I declare that I have no potential conflicts of interest

Introduction

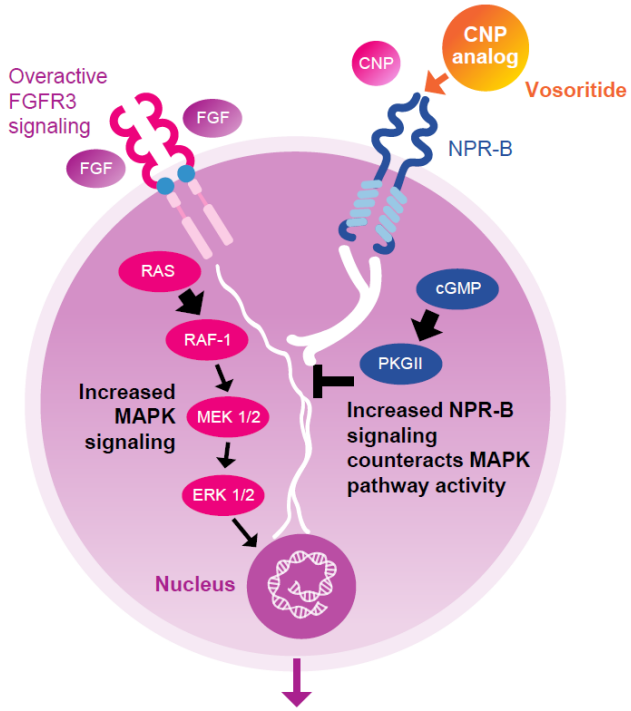
- In June 2022, Japan was the first country to approve vosoritide for use from birth through epiphyseal closure,[1,2] followed by subsequent approvals in the US and Australia[3]
- The ongoing post-marketing safety surveillance study (study 111-604) is providing interim data on the safety and effectiveness of vosoritide in children with achondroplasia in Japan who initiated treatment ≤3 years of age

Achondroplasia without treatment



Diminished endochondral bone ossification and limited growth[4,5]

Achondroplasia with vosoritide treatment



Improved endochondral bone growth[6,7]

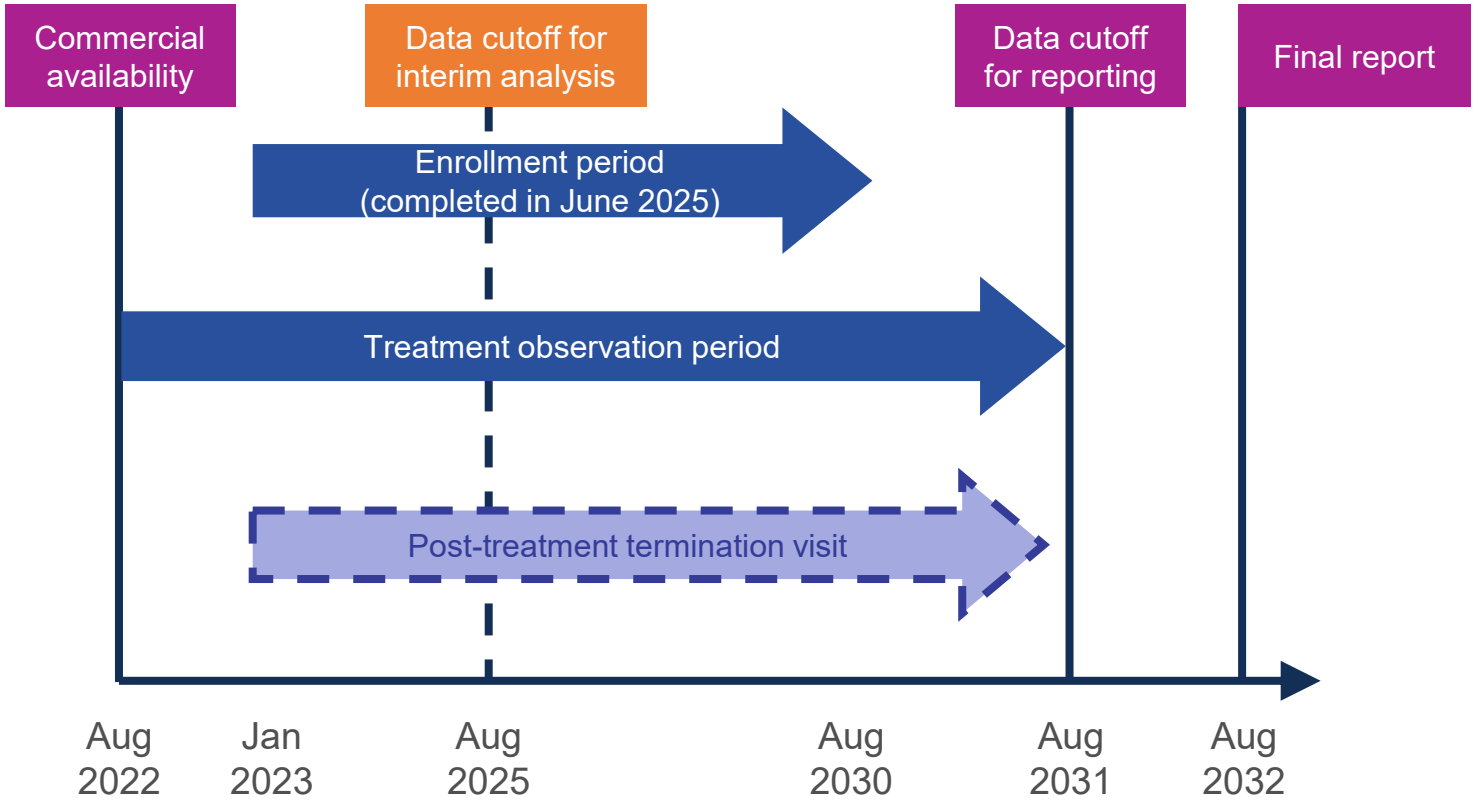
Objective: To report interim long-term safety and effectiveness of vosoritide in Japanese adolescents who initiated treatment at ≤3 years of age in 111-604

1. BioMarin announces the Ministry of Health, Labor and Welfare (MHLW) in Japan granted approval for VOXZOGO® (vosoritide) for injection for the treatment of children with achondroplasia, whose growth plates are not closed. BioMarin Pharmaceutical Inc. June 21, 2022. Accessed July 16, 2026. https://investors.biomarin.com/news/news-details/2022/BioMarin-Announces-the-Ministry-of-Health-Labor-and-Welfare-MHLW-in-Japan-Granted-Approval-for-VOXZOGO-vosoritide-for-Injection-for-the-Treatment-of-Children-with-Achondroplasia-Whose-Growth-Plates-are-Not-Closed-06-21-2022/default.aspx **2.** Michigami T, et al. *Genet Med Open.* 2025;3(suppl 2):102173. **3.** U.S. Food and Drug Administration Accepts BioMarin's Supplemental New Drug Application for Full Approval of VOXZOGO® (vosoritide) for Children With Achondroplasia. BioMarin Pharmaceutical Inc. July 13, 2026. Accessed July 29, 2026. https://www.prnewswire.com/news-releases/us-food-and-drug-administration-accepts-biomarins-supplemental-new-drug-application-for-full-approval-of-voxzogo-vosoritide-for-children-with-achondroplasia-302823072.html **4.** Foreman PK, et al. *Am J Med Genet A.* 2020;182(10):2297–316. **5.** Savarirayan R, et al. *Nat Rev Endocrinol.* 2022;18(3):173–189 **6.** Holmes G, et al. *PLoS One.* 2018;13(7):e0201492. **7.** Savarirayan R, et al. *Nat Rev Endocrinol.* 2025;21(5):314–24.

cGMP, cyclic guanosine monophosphate; CNP, C-type natriuretic peptide; ERK, extracellular signal-regulated kinase; FGF, fibroblast growth factor; FGFR3, fibroblast growth factor receptor 3; MAPK, mitogen-activated protein kinase; MEK, mitogen-activated protein kinase kinase; NPR-B, natriuretic peptide receptor-B; PKGII, cGMP-dependent protein kinase II; RAF1, rapidly accelerated fibrosarcoma-1; RAS, rat sarcoma.

Study design

- Study 111-604 is collecting prospective data beginning August 2022 from the medical records of children and adolescents with achondroplasia who have been prescribed vosoritide in Japan
- This analysis includes children who initiated treatment at ≤3 years of age



Adherence

- Treatment interruptions

Safety[a]

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

Efficacy

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

[a]Coded using MedDRA/J version 28.0. [b]Height Z-scores were referenced to age- and sex-matched children of average stature (CDC)[1] or untreated children with achondroplasia (CLARITY).[2]

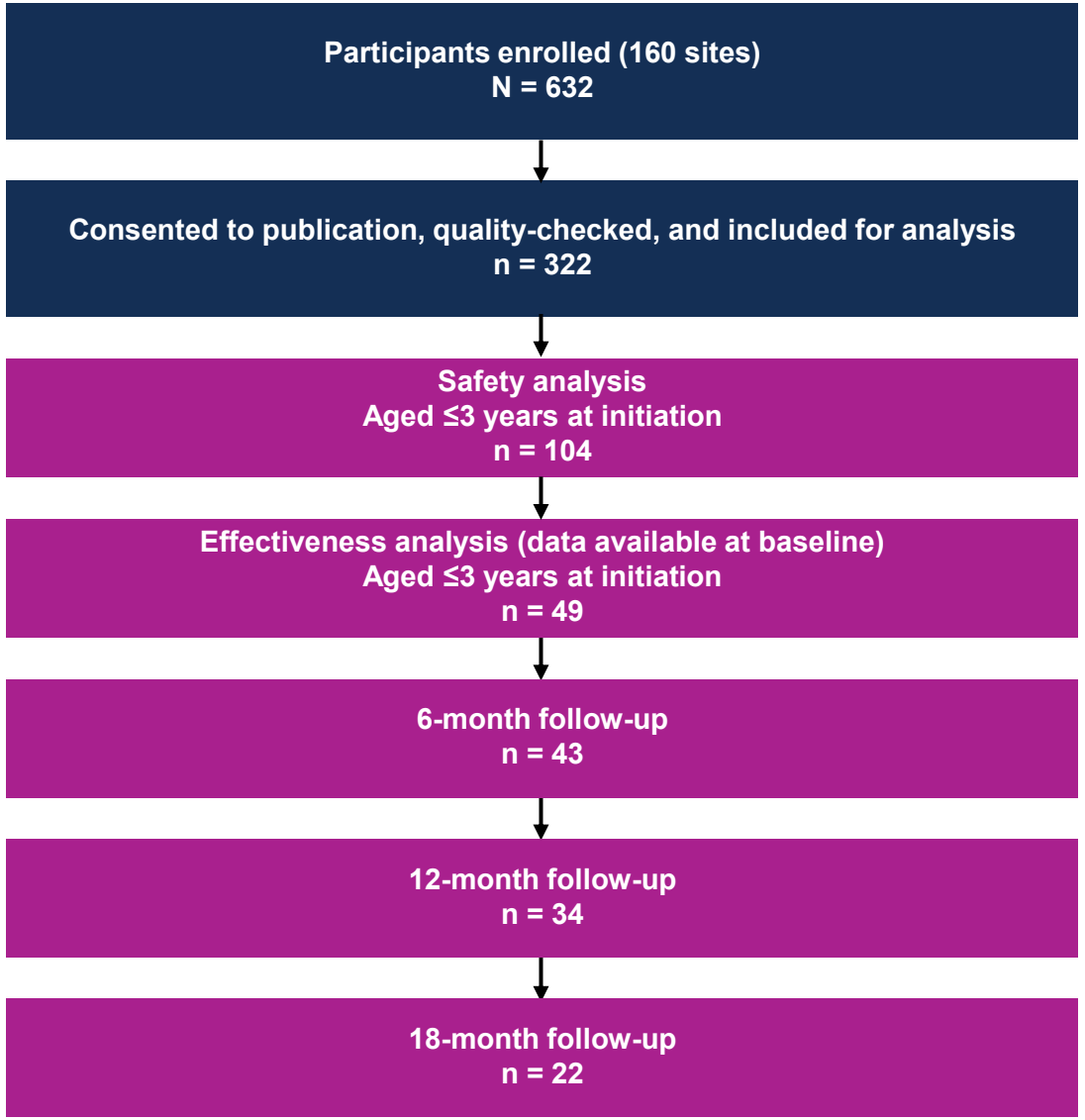
1. US Centers for Disease Control and Prevention. CDC growth charts. National Center for Health Statistics. Accessed January 29, 2026. https://www.cdc.gov/growthcharts/clinical_charts.htm. **2.** Hoover-Fong JE, et al. *Orphanet J Rare Dis*. 2021;16(1):522.

CDC, US Centers for Disease Control and Prevention; MedDRA/J, Japanese translation of Medical Dictionary for Regulatory Activities.

Participant disposition

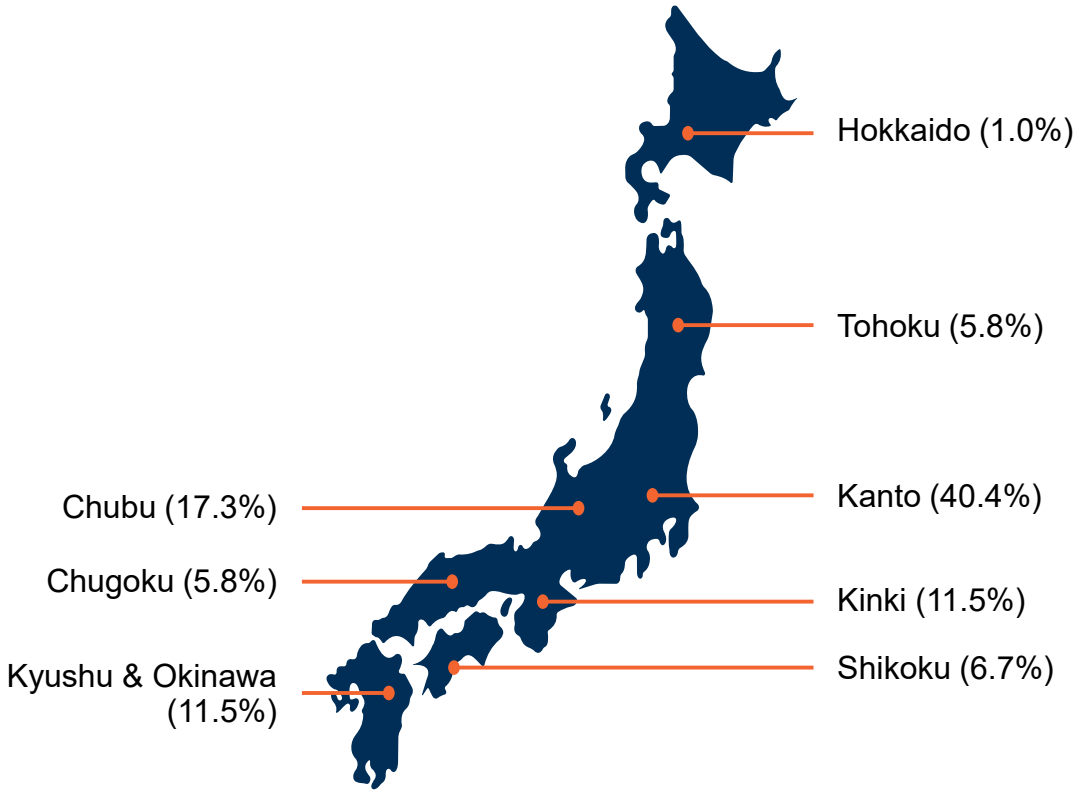
As of the August 25, 2025, data cutoff, 104 participants were aged ≤3 years at treatment initiation and included in this analysis





Geographic distribution, baseline characteristics, and adherence

Study participants were enrolled across all 8 regions of Japan



	Participants aged ≤3 years (N = 104)
Sex, n (%)	
Male	51 (49.0)
Female	53 (51.0)
Age at treatment initiation, months, mean ± SD	
Mean ± SD	12.9 ± 10.9
Median (range)	10.0 ± (0.0–36.0)
Prior growth hormone use, n (%)	0
Growth parameters, mean ± SD	
Standing height, cm	60.32 ± 8.88
Height Z-score (CDC-referenced)	−3.48 ± 1.54
Height Z-score (achondroplasia-referenced)	−0.04 ± 1.01
Follow-up duration, months	
Mean ± SD	25.0 ± 9.2
Median (range)	28.1 (4.1–35.7)
Treatment discontinuation, n (%)	2 (1.9)
Due to safety events	1 (1.0)
Other	1 (1.0)
Treatment interruption (missed 11 days of daily treatment), n (%)	1 (1.0)

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

Vosoritide demonstrates a favorable safety profile in children aged 3 years or younger

Two (1.9%) participants reported adverse drug reactions

- Worsening foramen magnum stenosis (1.0%)
- Injection-site pain (1.0%)

Three (2.9%) participants had bone/joint-related events. No participants had events associated with blood pressure reduction

Three (2.9%) participants reported serious safety events

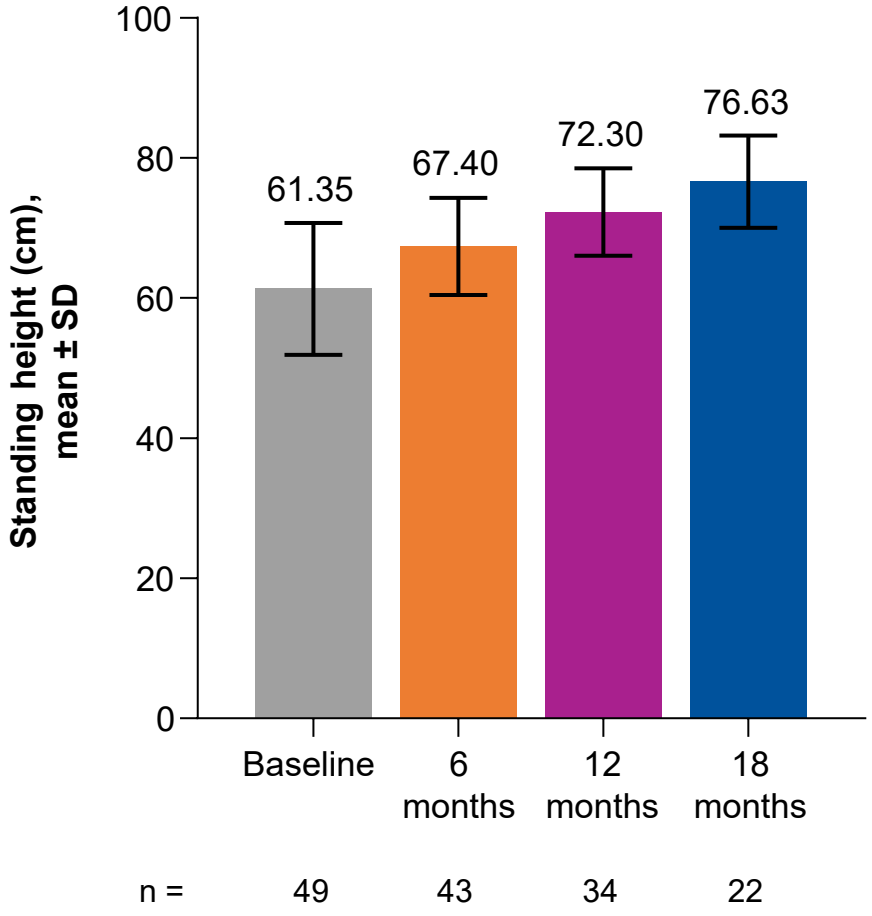
- Bronchitis (1.0%)
- Respiratory syncytial virus infection (1.0%)
- Abdominal distension (1.0%)
- Foramen magnum stenosis (1.0%)

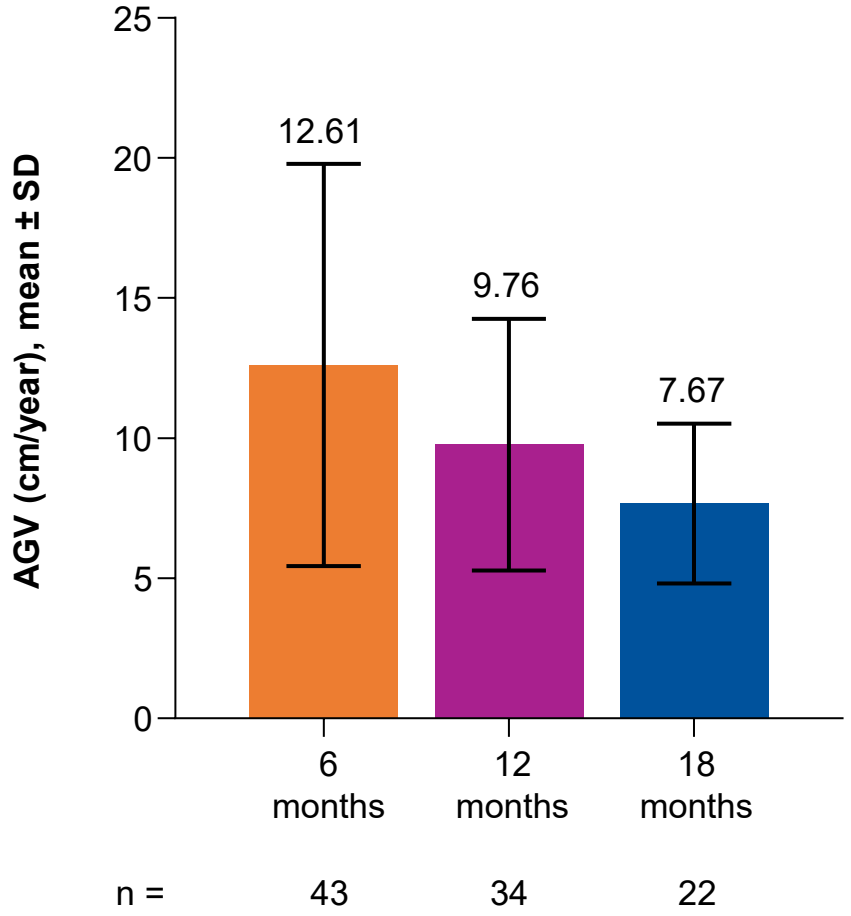
Thirteen (12.5%) participants had achondroplasia-related surgical events

- Foramen magnum decompression (6.7%)
- Myringotomy tubes (3.8%)
- Adenoidectomy (2.9%)
- Tonsillectomy (1.0%)
- Tympanostomy (1.0%)

N = 104 for safety analysis.

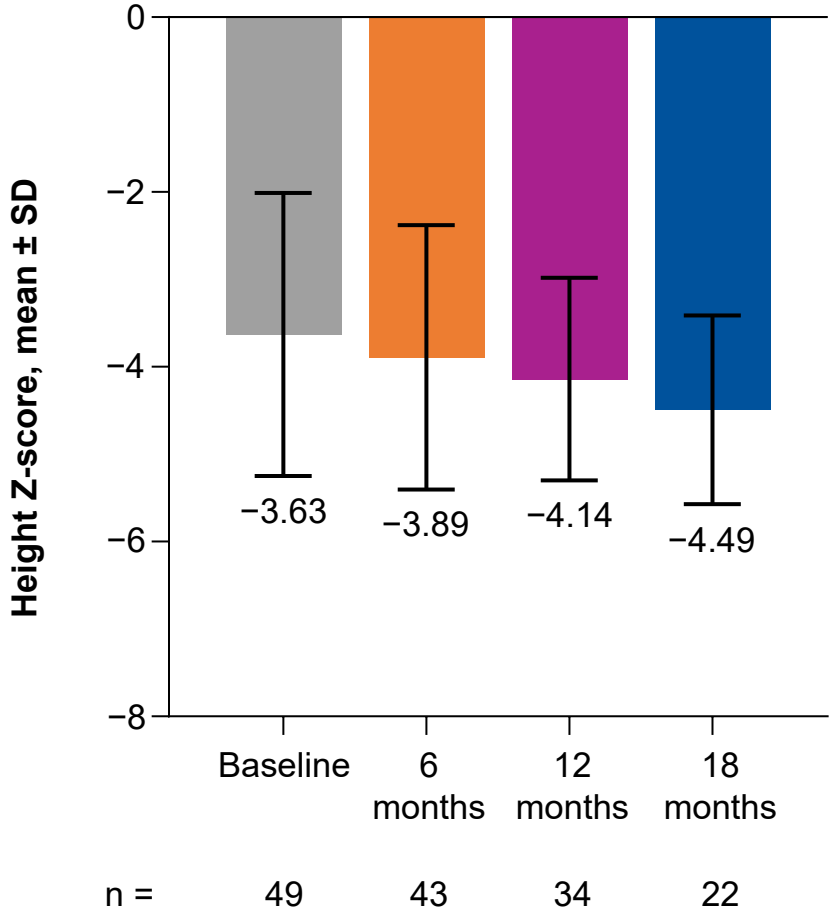
Increases in standing height and consistent cumulative AGVs were observed at 6, 12, and 18 months

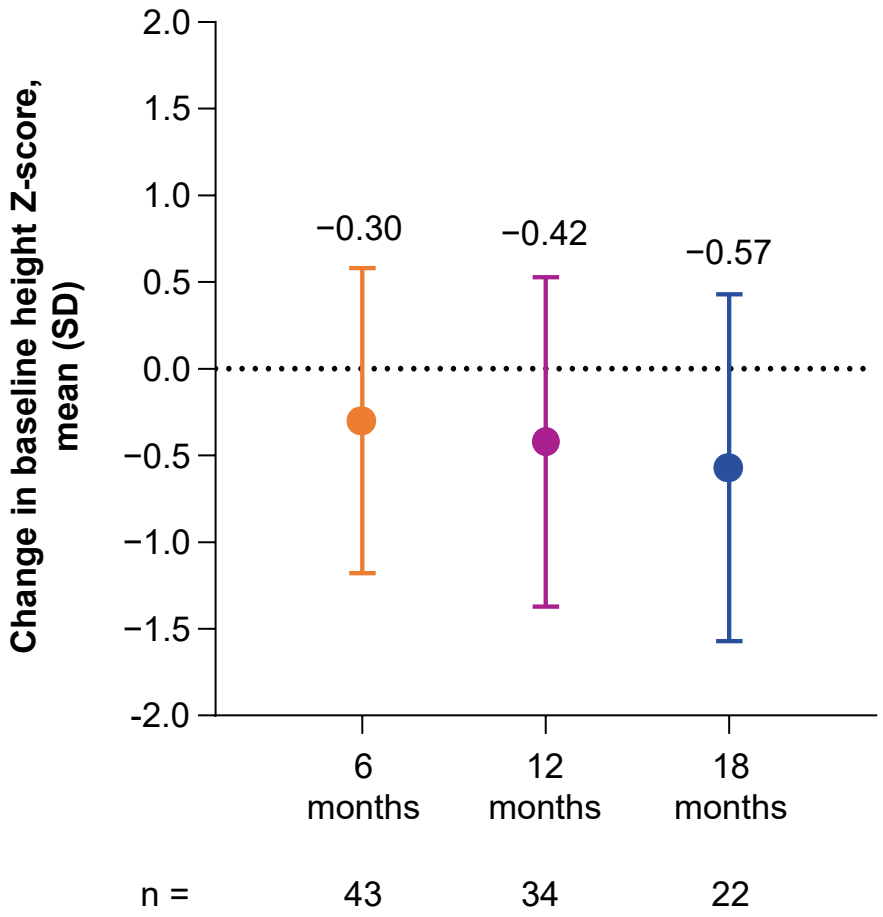




AGV, annualized growth velocity; SD, standard deviation.

Height Z-scores at 6, 12, and 18 months of follow-up: Average stature–referenced



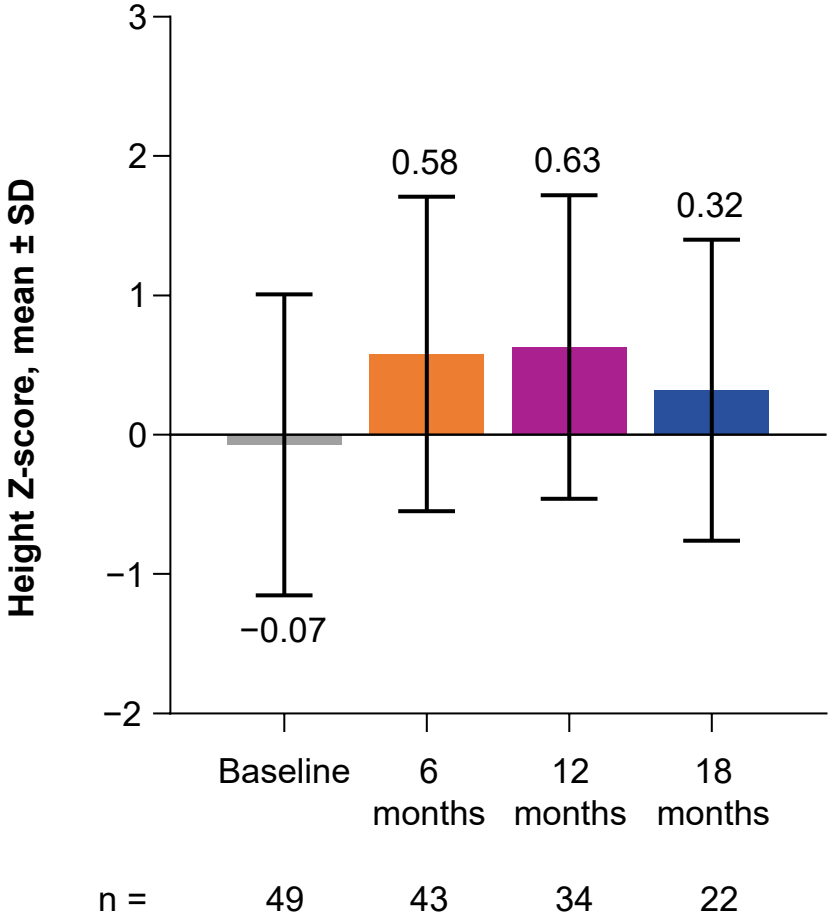


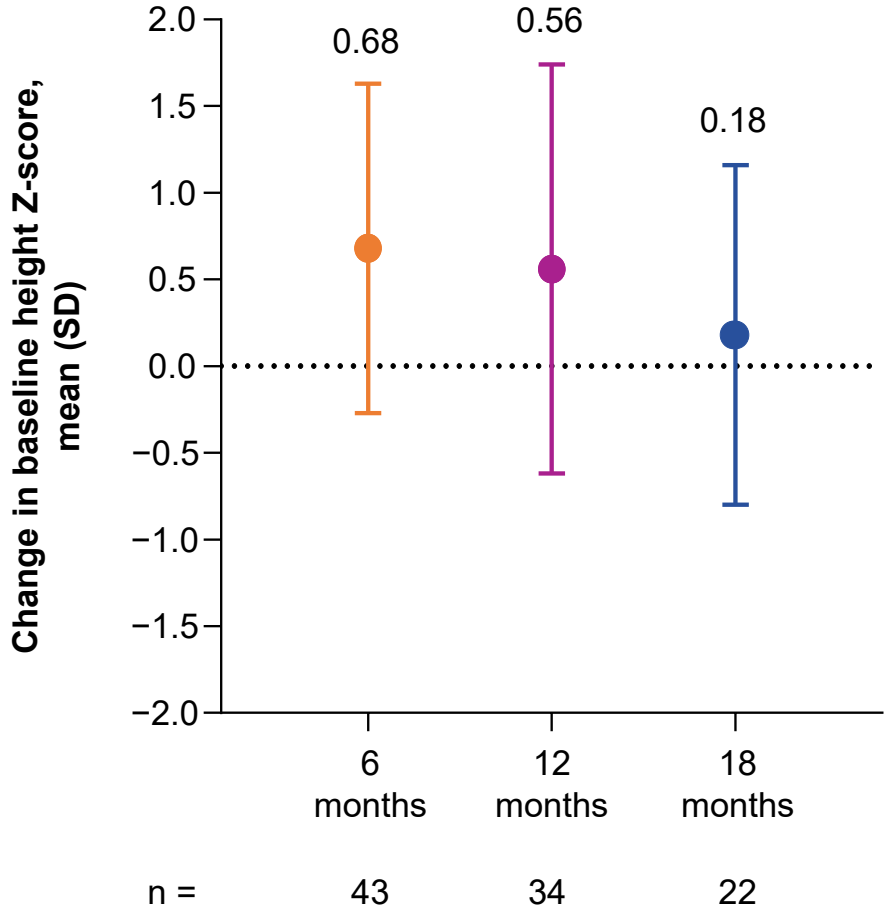
Height Z-scores were referenced to age- and sex-matched children of average stature (CDC).[1]

1. US Centers for Disease Control and Prevention. CDC growth charts. National Center for Health Statistics. Accessed January 29, 2026. https://www.cdc.gov/growthcharts/clinical_charts.htm

SD, standard deviation.

Height Z-scores at 6, 12, and 18 months of follow-up: Achondroplasia-referenced





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 treated from ≤3 years of age



Early initiation of vosoritide was associated with improved growth outcomes, including improvements in height and achondroplasia-referenced Z-scores



These interim data are consistent with clinical trial data and support the effectiveness and safety of vosoritide treatment in Japanese children from birth through adolescence

Acknowledgments

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