P2-56

Real-world effectiveness of vosoritide in children with achondroplasia: Results from 18 months follow-up in France

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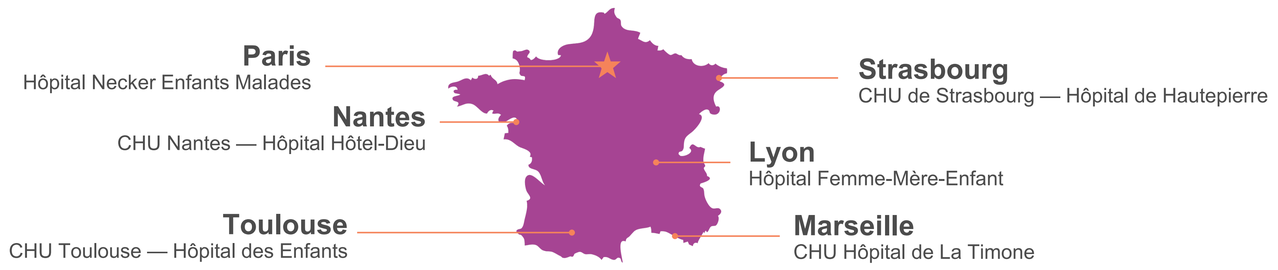
Introduction

- Achondroplasia (ACH), the most common skeletal dysplasia, is caused by gain-of-function variants of the fibroblast growth factor receptor 3 (*FGFR3*) gene[1,2]
- Vosoritide, a recombinant C-type natriuretic peptide that stimulates endochondral bone growth by downregulating FGFR3 signalling, has been approved by the European Medicines Agency for children age ≥4 months until closure of epiphyses[3]
- The first participants treated with vosoritide outside of a clinical trial did so through a pre-marketing authorization early access programme (EAP) in France that began in June 2021, transitioned to a post-marketing authorization in December 2021, and ended when commercialization began in France on 13 December 2022
  - Effectiveness and safety data were collected for 12 months of follow-up and were previously reported[4]
- Here, we report real-world effectiveness data collected post hoc over 18 months of follow-up in the early access programme in France

Methods

The vosoritide EAP was conducted by a consortium of ACH experts within the French Rare Disease reference centres for Constitutional Bone Diseases (MOC) at the coordinating MOC centre at Paris and 5 other MOC centres in France



Eligible participants were children with genetically confirmed ACH age ≥5 years with open epiphyses

Participants received 15 µg/kg vosoritide subcutaneously once daily

Follow-up visits took place 1, 3, and 6 months after treatment initiation and every 6 months thereafter

The effectiveness of vosoritide for participants for whom at least 18 months of data were available (6 months after the end of the early access programme) is presented here

Effectiveness endpoints

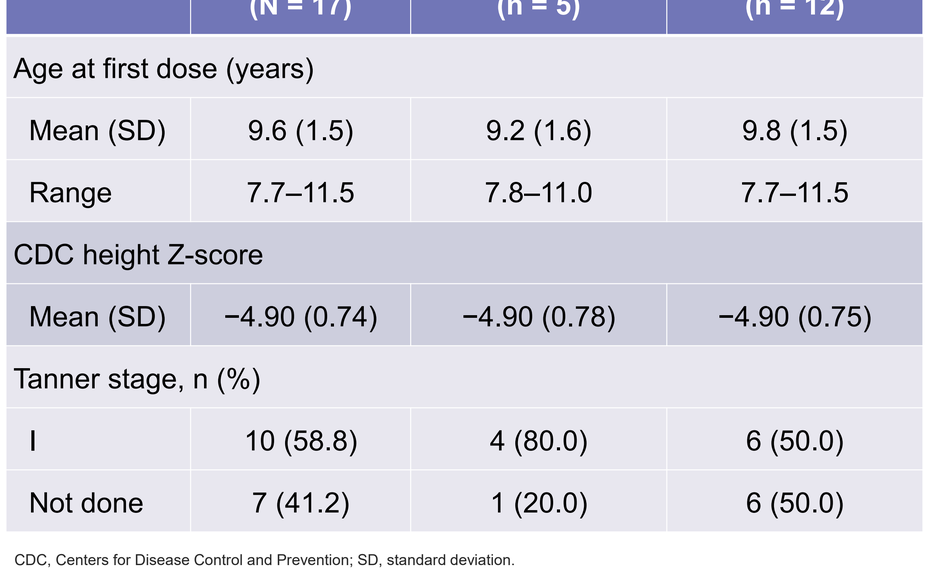
- Height
- CDC height Z-score[a]
- ACH height Z-score[b]
- AGV

[a]Referenced to the population with average stature with data from the CDC.[5]
[b]Referenced to natural history data from children with untreated ACH.[6]
ACH, achondroplasia; AGV, annualized growth velocity; CDC, Centers for Disease Control and Prevention; CHU, University Hospital Centre.

Results

Participants

- At least 18 months of effectiveness data were available for 17 participants



EAP, early access programme.

Baseline demographics and clinical characteristics

	Treated ≥18 months (N = 17)	Males treated ≥18 months (n = 5)	Females treated ≥18 months (n = 12)
Age at first dose (years)			
Mean (SD)	9.6 (1.5)	9.2 (1.6)	9.8 (1.5)
Range	7.7–11.5	7.8–11.0	7.7–11.5
CDC height Z-score			
Mean (SD)	−4.90 (0.74)	−4.90 (0.78)	−4.90 (0.75)
Tanner stage, n (%)			
I	10 (58.8)	4 (80.0)	6 (50.0)
Not done	7 (41.2)	1 (20.0)	6 (50.0)

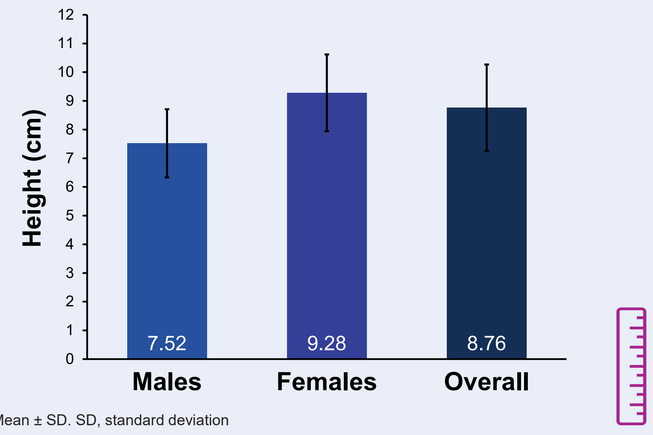
CDC, Centers for Disease Control and Prevention; SD, standard deviation.

- Baseline demographics were generally similar between male and female participants treated for at least 18 months
- To maximize the opportunity for vosoritide treatment before commercialization, the experts leading the EAP prioritised enrolment of older participants; thus, participants with at least 18 months of follow-up were slightly older (mean age, 9.6 years; standard deviation [SD], 1.5 years) than the overall sample (mean age, 8.6 years; SD, 2.0 years)
- Mean (SD) treatment exposure was 19.17 (2.01) months (range, 12.82–21.86 months)

Effectiveness

Participants experienced growth after 18 months of treatment, with greater numerical height gains in females compared with males

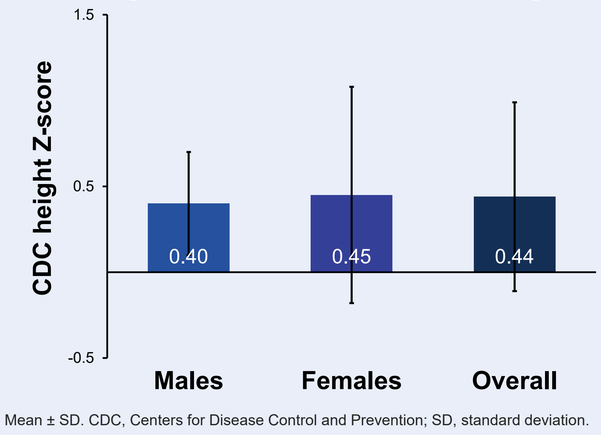
Change from baseline in height



Mean ± SD. SD, standard deviation

Height Z-score improved in males and females after 18 months of vosoritide treatment compared with a reference population of children of average stature[5]

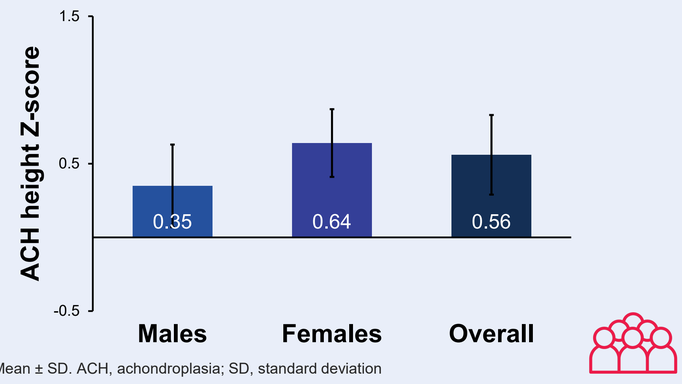
Change from baseline in CDC height Z-score



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

Height Z-score improved compared with a reference population of untreated children with ACH after 18 months of vosoritide treatment, with a greater numerical increase in females compared with males[6]

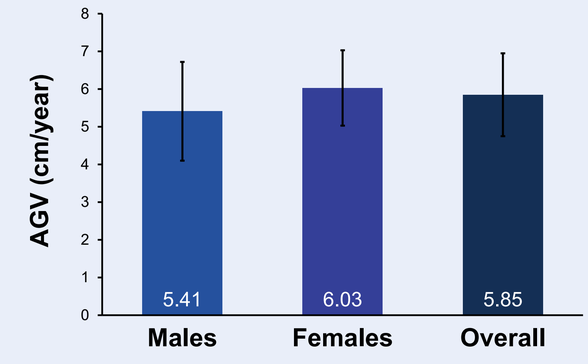
Change from baseline in ACH height Z-score



Mean ± SD. ACH, achondroplasia; SD, standard deviation

After 18 months of treatment, AGV was similar for male and female participants

AGV at month 18



Mean ± SD. AGV, annualized growth velocity; SD, standard deviation.

Conclusions

- These data demonstrate the durability of treatment response in real-world use, with improvements from baseline in height and AGV as well as height Z-scores referenced to children of average stature and children with untreated ACH
- As reported previously, vosoritide was well tolerated, with only mild adverse events for up to 12 months of follow-up[4]
- These results are consistent with a phase 3 clinical trial of vosoritide in which treatment improved stature and growth rate for up to 2 years in children with ACH between the ages of 5 and <18 years[7,8]

References

1. Pauli RM, et al. *Orphanet J Rare Dis*. 2019;14(1):1. **2.** Savarirayan R, et al. *Nat Rev Endocrinol*. 2022;18(3):173–89. **3.** European Medicines Agency. Voxzogo product information. Accessed August 2024. **4.** Cormier-Daire V, et al. Poster presented at European Society for Paediatric Endocrinology, 21–23 September 2023. **5.** Centers for Disease Control and Prevention NCfHS. CDC growth charts: United States. **6.** Hoover-Fong J, et al. *Mol Genet Metab*. 2021;132:S101. **7.** Savarirayan R, et al. *Lancet*. 2020;396(10252):684–92. **8.** Savarirayan R, et al. *Genet Med*. 2021;23(12):2443–7.

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Disclosures

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