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Real-world experience with vosoritide for achondroplasia: Interim findings from an early access programme in France

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Background and Objectives

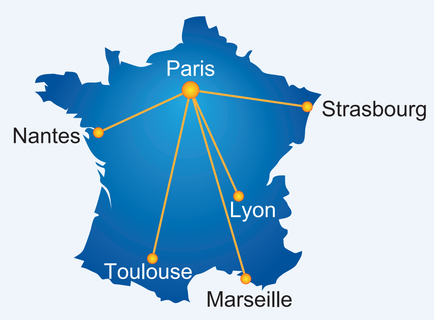
- Achondroplasia (ACH) is the most common form of disproportionate short stature (approx. 1:25,000 live births)[1,2]
- ACH is caused by a pathogenic mutation in the *FGFR3* gene, leading to impaired endochondral bone growth and multiple medical complications[1,3]
- Vosoritide is a CNP analogue that leverages the CNP pathway to counteract overactive *FGFR3* signaling and stimulate endochondral bone growth[4,5,6]
- On 26 August 2021, the European Medicines Agency (EMA) approved vosoritide (once daily, subcutaneous injection) for treating ACH in patients aged ≥2 years until closure of epiphyses
- Prior to this, vosoritide was made available through a cohort Temporary Authorization for Use (ATUc), approved by the National Agency for the Safety of Medicines and Health Products (ANSM) on 24 June 2021
- After EU approval, at the request of the French authorities the ATU cohort transitioned to an Approved Authorized Early Access 2 (AAP2), in December 2021
- We report the first interim findings from this real world access programme

Methods

- A consortium of French ACH experts (CRMR MOC) reviewed ACH cases followed in the network, to confirm eligibility for treatment initiation with vosoritide
- ANSM approved the ATU for children ≥5 years with open epiphyses, and the CRMR MOC prioritized the enrolment of older patients
- After treatment initiation and parent therapeutic education, patients were followed up via visits at month 1, 3 and 6 and at 6-monthly intervals thereafter
- Data were collected to evaluate treatment compliance, adverse events and growth
- Analyses were performed on a datacut from 8 August 2022

Participating centers

ATU Center
Hôpital Necker Enfants Malades, Paris
CHU Toulouse – Hôpital des Enfants, Toulouse
CHU Nantes – Hôpital Hôtel-Dieu, Nantes
CHU de Strasbourg – Hôpital de Hautepierre, Strasbourg
Hôpital de La Timone, Marseille
Hôpital Femme-Mère-Enfant, Lyon



Data collected at each visit

	Treatment access request	Day 0 visit (start of treatment)	Month 1	Month 3	Month 6, then every 6 months	End of follow-up
Documentation of ACH[a]	X					
Demographic data	X		X		X	
Physical examination	X			X (annual examination)		
Anthropometric and morphological measurements		X		X (annual examination)		
X-ray of the left hand and/or knee[b]	X			X (annual examination)		
Stage on the Tanner Scale		X[c]	X	X	X	X[c]
Vosoritide treatment			X	X	X	X
Adverse event data[d]		X	X	X	X	X

[a]Documentation includes the patient's age at diagnosis, the place and author of the diagnosis, and confirmation of genetic testing.
[b]From 7 years of age. Only if this examination is performed as part of recommended treatment.
[c]Prepubertal stage without closure of the epiphyseal cartilage in patients aged 7 to 12 years.
[d]All safety events were reported to BioMarin within 24 hours of identification.

Results

- The first patient enrolled in the ATU on 8 September 2021 and was treated on 27 September 2021
- 48 patients were enrolled from 6 centres across France and 46 have initiated treatment with vosoritide
  - There were 43 patients with follow-up data available at month 1, 31 patients at month 3, and 30 patients at month 6
- Analyses were conducted among 46 treated patients

Demographics at start of treatment (Day 0)

	Overall treated (n=46)
Gender, n (%)	
Male	22 (47.8%)
Female	24 (52.2%)
Age at first dose (years)	
Mean (SD)	8.9 (1.91)
Range	5, 13
Height Z-score Mean (SD)	
Male (n=21)	-5.1 (1.08)
Female (n=22)	-4.7 (1.05)
Overall (n=43)	-4.9 (1.07)
Weight (kg) Mean (SD)	
Male (n=21)	23.3 (6.57)
Female (n=23)	23.4 (5.24)
Overall (n=44)	23.3 (5.84)
Tanner Stage n (%)	
I	25 (54.3%)
II	2 (4.3%)
III	0
IV	0
V	0
Missing	19 (41.3%)

SD: Standard deviation of the mean.

Radiological Exam Results

- At study entry, there were no reports of patients with complete closure of epiphyses
- Not all patients recorded baseline radiographic examination results; 31 reported open hand epiphyseal growth plates and 16 reported open knee epiphyseal growth plates

Treatment Exposure and Adherence

Duration on treatment

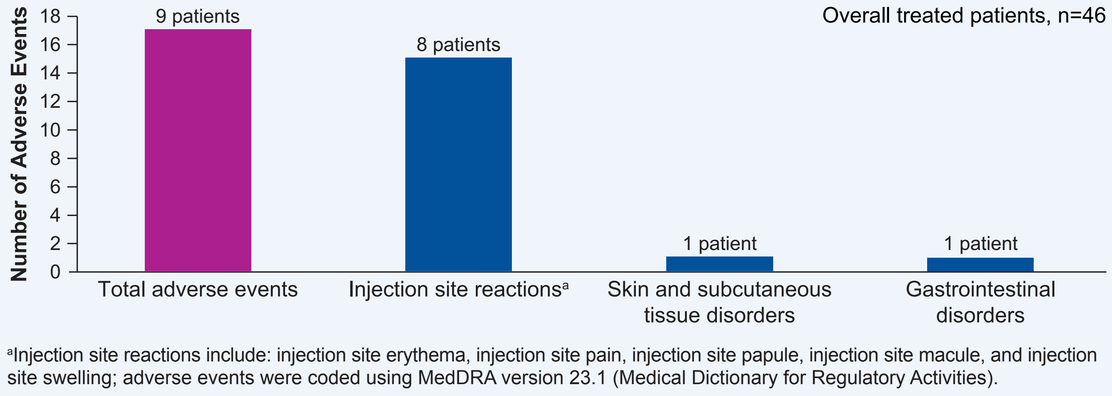
Exposure to vosoride (days)	Overall treated (n=46)
Cumulative exposure	9334
Mean (SD)	202.9 (109.24)
Range	29, 316

- Duration of treatment follow-up ranged from just less than 1 month to approximately 11 months
- No patients discontinued treatment
- A total of 7 patients missed a total of 13 doses overall

Safety

- In total, there were 17 adverse events (AEs) reported among 9 patients
- The majority of AEs were mild and included injection site reactions and vomiting
- The most common AE was injection site papules (6 events)
- There were no serious adverse events related to vosoritide treatment

Adverse events



[a]Injection site reactions include: injection site erythema, injection site pain, injection site papule, injection site macule, and injection site swelling; adverse events were coded using MedDRA version 23.1 (Medical Dictionary for Regulatory Activities).

Conclusions

- In France, enrolment of patients in this early access program has been encouraging, with all patients demonstrating good adherence and remaining on treatment
- Over almost 12 months, the safety profile of vosoritide in children with ACH was consistent with that observed in clinical trials[5,6,7]
- Future analyses will additionally include effectiveness measures (annual growth velocity and change in Z-score) after 1 year follow-up assessments are available
- The outputs from this early access programme will continue to establish the safety and effectiveness of vosoritide in the real world

References

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