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Design and objectives of the Acorn study: a non-interventional study evaluating long-term safety in children with achondroplasia treated with vosoritide

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Acorn
ACHONDROPLASIA RESEARCH

Background

- Achondroplasia (ACH) is a rare skeletal dysplasia caused by a pathogenic variant in the fibroblast growth factor receptor 3 gene (*FGFR3*), leading to impaired endochondral bone growth and multiple medical complications[1,2]
- Vosoritide, a modified recombinant human C-type natriuretic peptide is approved by the European Medicines Agency (EMA) for treating ACH in children aged ≥4 months with a genetically confirmed diagnosis until closure of epiphyses[3]

- Acorn is the first treatment-based registry for ACH that monitors real-world, long-term use of vosoritide
- Here we describe the methodology, objectives, and preliminary data from the Acorn study

Methods

Study design

- Acorn (European post-authorization study registration, EUPAS47514) is a real-world, observational, prospective, multicentre, non-interventional, post-authorization, category 3 safety study (**Figure 1**)

Figure 1. Acorn study design

Participant screening
Distinguish between incident (cohort 1) and prevalent (cohort 2) users

Study enrolment
Establish cohort 1 and cohort 2

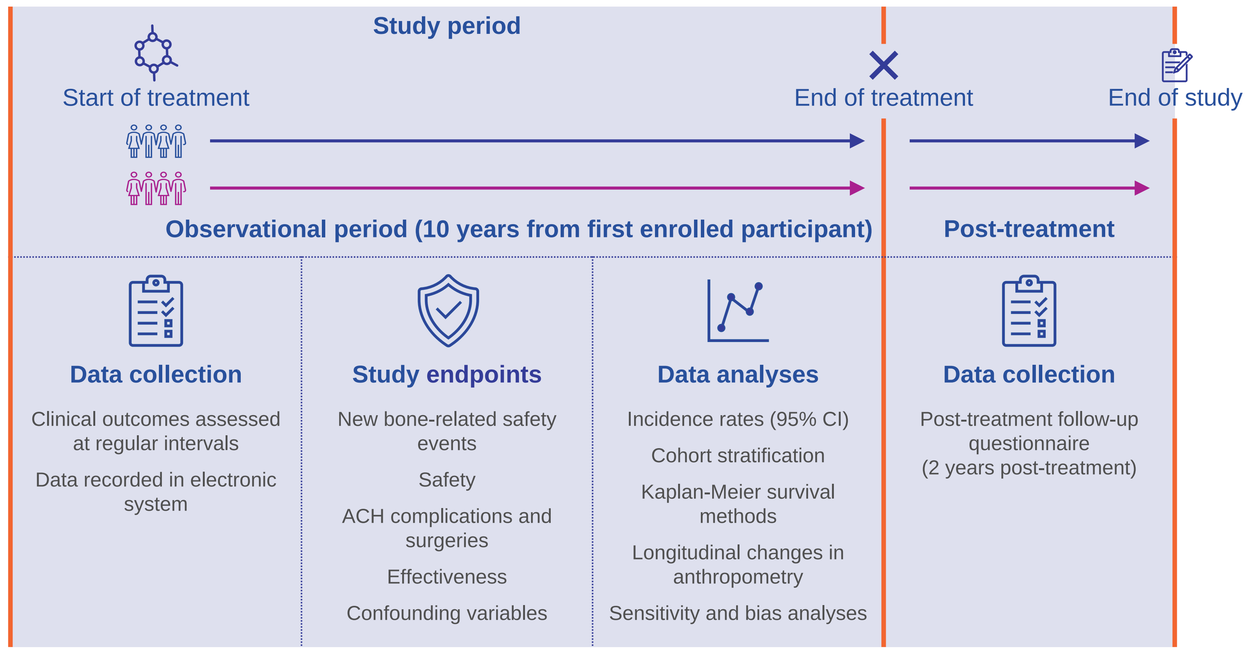
Cohort 1 is considered the primary analysis group

Cohort 1 Incident users

Cohort 1 inclusion criteria
- Aged ≥4 months to ≤8 years old
- Recently started vosoritide treatment or plan to initiate treatment within 3 months of enrolment
- Anticipation of ≥36 months of vosoritide treatment during the study

Cohort 2 Prevalent users

Cohort 2 inclusion criteria
- Initiated treatment in the French EAP or vosoritide open-label clinical trials and have discontinued and switched to commercial vosoritide treatment and do not meet cohort 1 inclusion criteria
- Anticipation of ≥36 months of vosoritide treatment, comprising time in French EAP/prior clinical trials and the current study



CI; confidence interval; EAP, expanded access program.

Study objectives

	Objectives	Endpoints
Primary	To evaluate the long-term impact of vosoritide treatment on **adverse bone-related safety events**	▪ Fractures ▪ Slipped capital femoral epiphysis ▪ Osteonecrosis or avascular necrosis ▪ Spinal cord and nerve root disorder ▪ Spine and neck deformities ▪ Joint disorder (eg, joint contractures, joint laxity hypermobility, genu varum) ▪ Clinically apparent cartilage disorder
Secondary	Assess the long-term impact of treatment with vosoritide on **safety and disease-related outcomes**	▪ SAEs, severe ADRs, and ADRs leading to treatment discontinuation ▪ Surgeries related to bone-related safety events of interest ▪ ACH-related complications and surgeries (excluding elective limb-lengthening surgeries) ▪ Changes in anthropometric measures, including height
	Evaluate the **immunogenic potential** of vosoritide treatment	▪ Severe injection-site reactions ▪ Vosoritide-related hypersensitivity events
	Understand surgical outcomes and treatment experiences in patients who undergo **elective bone-related surgery**	▪ Treatment interruption or discontinuation ▪ Complications, length of hospital stay, infections, and antibiotic use

ACH, achondroplasia; ADR, adverse drug reaction; SAE, serious adverse event.

Preliminary results

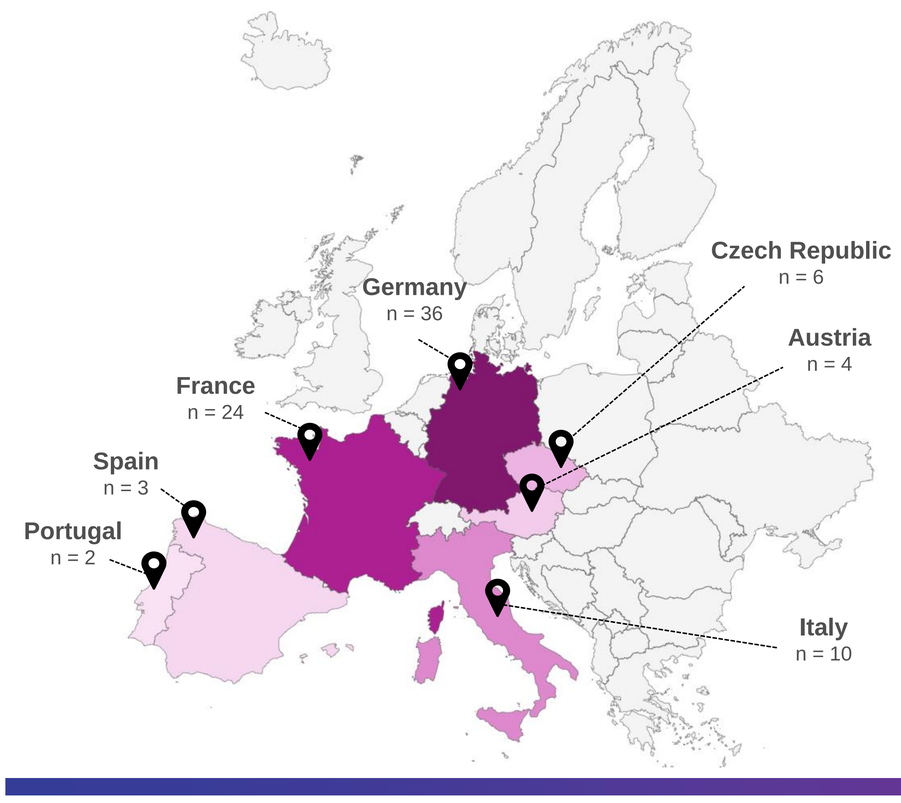
Study participation

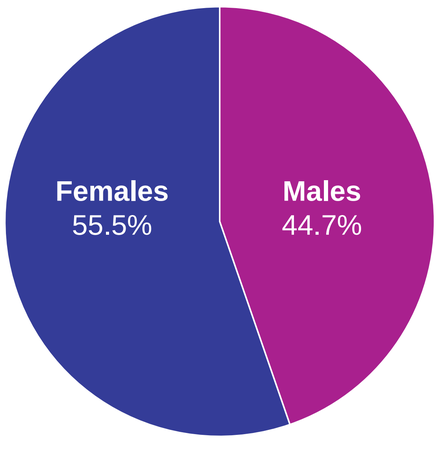
- As of 11 July 2024, 85 participants were enrolled from 17 sites in 7 countries (**Figure 2**); participation numbers are expected to increase as enrolment continues

Cohort 1
67 participants were assigned to **cohort 1**

Cohort 2
11 participants were assigned to **cohort 2**

Figure 2. Pan-European participation in the Acorn study





Treatment outcomes

- Preliminary data from enrolled participants indicated mean (standard deviation [SD]) age at enrolment was 6.5 (3.3) years
- Participants have been receiving vosoritide for a mean (SD) duration of 16.2 (9.4) months
- No bone-related safety events reported
- No participants have discontinued treatment
- There have been no treatment interruptions or missed doses (a missed dose is defined as no dose for 7 consecutive days) among available treatment data (n = 74)

Conclusions

- Vosoritide is the first approved medicinal treatment for children with ACH
- Acorn is collecting real-world data across Europe and will provide important insights on long-term safety and effectiveness of vosoritide and use in the context of other interventions
- Expansion of the indication to ≥4 months will now allow enrolment of younger participants
- Vosoritide treatment is well tolerated, with no reported discontinuations or interruptions to date

References

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Disclosures

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