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Design and objectives of Study 111-902: a multicenter, prospective, and retrospective observational study of children with hypochondroplasia

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Introduction

- Hypochondroplasia (HCH), a rare genetic skeletal condition, is caused by gain-of-function variants in *FGFR3* that lead to decreased endochondral bone growth, disproportionate short stature, and multisystem complications[1,2]
- HCH shares pathogenetic and phenotypic similarities with achondroplasia (ACH) but generally has a less severe clinical presentation
- Current management of HCH is limited to supportive care and surgery
- Vosoritide, a C-type natriuretic peptide analog, is an approved first-in-class targeted treatment for ACH that is now being investigated in HCH[3,4]
- Here, we present the design of Study 111-902 (NCT06212947), a non-interventional study to generate natural history data, as well as baseline growth data to support interventional studies of vosoritide for HCH[5]

Conclusions

- Study 111-902 will collect longitudinal growth measurements and other variables, including specific medical events, frequency and nature of interventions, and the impact of HCH on quality of life
- Important insights into the clinical manifestations and course of HCH in children will be gained, enabling the natural history of this condition to be further delineated
- Prospective growth measurements collected in this study for at least 6 months will serve as baseline data for future interventional studies of vosoritide in HCH

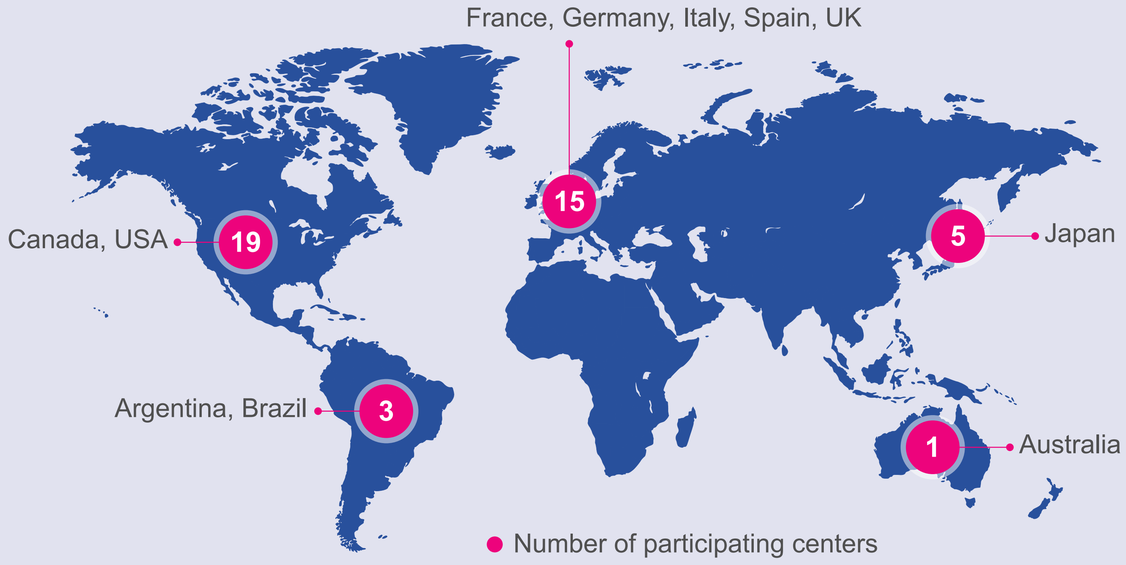
Study 111-902

Objective

- To assess growth over time in children with HCH across all ages and by sex, the impact on HRQoL measures, and rate and burden of comorbidities, interventions and procedures

Design

- Study 111-902 is a multicenter, multinational, prospective, and retrospective observational study
- Prospective growth data will be collected for a minimum of 6 months; retrospective data extraction will provide previous growth measurements and medical history
- No investigational drug is being administered during the study



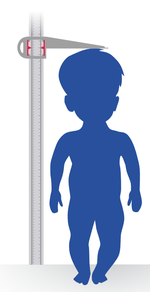
Population

- ✓ Aged ≤15 years at the time of consent
- ✓ Genetic confirmation of HCH diagnosis
- ✗ Diagnosis of a genetic short stature condition other than HCH or other condition associated with short stature
- ✗ Received an investigational product or medical device within 6 months before the screening visit

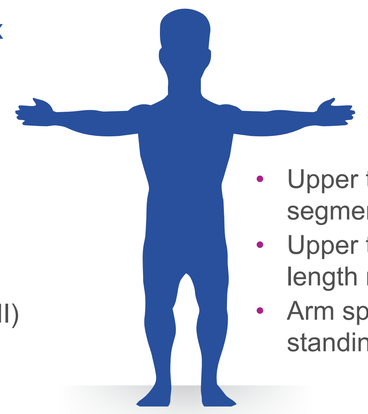
Key measures

Every 6 months

Data summarized by age and sex



- Annualized growth velocity
- Height
- Height Z-score
- Body mass index (BMI)
- BMI Z-score



- Upper to lower body segment ratio
- Upper to lower leg length ratio
- Arm span to standing height ratio

Every 12 months

Data summarized by age and sex

- Health-related quality of life, including QoLISSY physical domain and total scores
- Frequency, rate, and burden of medical events, interventions, and procedures

- Maximum study duration for participants is defined by the achievement of final adult height (FAH)
- In consenting participants, the association between genomic variants and outcomes such as growth and FAH will be explored

After 6 months, participants may enroll in the 52-week Phase 3, randomized, stratified, placebo-controlled study of vosoritide in HCH (NCT06455059)[5]

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Abbreviations

ACH, achondroplasia; BMI, body mass index; FAH, final adult height; *FGFR3*, fibroblast growth factor receptor 3 gene; HCH, hypochondroplasia; QoLISSY, Quality of Life in Short Stature Youth questionnaire

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