Background

- FOP is an ultra-rare genetic disorder with an estimated prevalence of up to 1.4 per million individuals.1
- The median age at diagnosis is 5 years, and individuals are supported by a range of medical specialties, including paediatric endocrinologists.
- FOP is characterised by progressive and heterotopic heterotopic ossification (HO).2
- HO develops into ribbons, sheets and plates of extra bone throughout the body and across joints, restricting movement; most individuals are immobilised by the third decade of life.3-5
- Individuals with FOP often develop tibial osteochondromas, broad femoral necks and progressive spinal deformities.6,7

Objective

To describe normal long bone growth, linear growth changes and incidence of bone abnormalities at epiphyseal plates in individuals with FOP aged <18 years enrolled in a 3-year NHS.

Methods

- Individuals with FOP with a documented ACVR1mutation aged ≥6 years were eligible to participate in a 36-month, global, prospective, protocol-defined NHS (NCT01322255, Figure 1).
- The analysis presented herein includes individuals aged >8 years at Baseline.
- Femur and tibia lengths, and abnormalities of hand/wrist and knee epiphyseal plates, were determined using low-dose whole-body computed tomography (WBCT).
- Knee height assessments were completed using a knee caliper.
- Linear growth assessments were completed using a stadiometer.

Figure 1. Natural history study design

CONCLUSIONS

- Younger participants aged <14 years at Baseline showed increases in femur and tibia length and knee height over 36 months, but these plateaued in older adolescent participants aged 14–18 years at Baseline.
- Knee height losses were likely due to difficulties obtaining accurate measurements in participants who struggled to maintain a seated position.
- Decreasing linear height z-scores highlight the difficulties associated with obtaining accurate growth measurements in younger individuals with FOP due to worsening skeletal deformities such as scoliosis, kyphosis and arthropy over time.
- The only growth plate abnormally identified was dense metaphyseal bands, the incidence of which appeared stable over 36 months.
- Comparatively low numbers of participants at Month 36 compared with Baseline limits comparison of the outcomes reported between age groups over 36 months.

Table 1. Baseline demographics and characteristics for participants ≥25 years

<table>
<thead>
<tr>
<th>Age, years, median (range)</th>
<th>Sex, male, (%)</th>
<th>Number of flare-ups within the 12 months prior to Baseline</th>
<th>Number of flare-ups within the 12 months prior to Baseline who struggled to maintain a seated position, median (range)</th>
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Abbreviations

ACVR1: activin A receptor type 1; FOP: Fibrodysplasia ossificans progressiva; RPs: Ranelted patients; NHS: natural history study; WHO: world health organisation.

References


Figure 2. Change from Baseline in normal long bone growth and knee height over 36 months in individuals with FOP by age group

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Figure 3. Change from Baseline in linear height z-scores over 36 months in individuals with FOP

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