Responder analysis of the Patient Life Interference questionnaire in children with growth hormone (GH) deficiency treated with either injections of once weekly GH (somatrogon) or once daily GH (Genotropin) in a phase 3 trial

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Objective

To conduct a responder analysis from data generated from a patient-reported outcome, the Patient Life Interference (PLI) questionnaire (primary endpoint), reported from patients with paediatric growth hormone deficiency (pGHD) in a phase 3 trial, to support and understand its interpretation.

Conclusions

A significantly higher proportion of patients treated with once-weekly somatrogon reported meaningful reductions in treatment burden (as shown by reduced PLI). This could lead to improved adherence and better outcomes compared to Genotropin once a day. These results support the phase 3 primary endpoint results.

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Background

Growth hormone deficiency (GHD) is characterized by inadequate secretion of growth hormone (GH); treatment with daily GH is standard of care.[1]

Somatrogon is a long-acting rhGH comprised of the amino acid sequence of hGH and 3 copies of the carboxy-terminal peptide (CTP) from human chorionic gonadotropin.[2] Phase 3 trial results in children with GHD demonstrated somatrogon to be well tolerated and demonstrated non-inferiority (efficacy outcome) to Genotropin.[3]

A separate phase 3 cross-over trial, comparing treatment burden of the once weekly regimen vs once daily Genotropin in pediatric GHD, demonstrated that patients had less treatment burden and had overall a better injection experience with the weekly schedule compared to daily treatments.[4]

Burden was evaluated using the Dyad Clinical Outcomes Assessment questionnaire (DCOA).[5] One section of the questionnaire evaluated 'Patient Life Interference' (PLI).

An anchor measure, the Patient Global Impression of severity-impact on daily activity (PGIS-IDA) was also administered.

Post-hoc responder analysis of PLI scores (via anchor-based approach) was conducted on patients who completed the patient PLI questionnaire at Baseline (BL), Week 12 & Week 24.

In this study, a responder was defined as having a lower PLI score.

Materials and Methods

This phase 3 (NCT03831880) open-label, crossover study randomised non-naïve patients with pGHD (3 to <18 years) 1:1 to receive: Sequence 1 or Sequence 2: 12 wks of somatrogon and 12 wks of Genotropin (Fig 1).

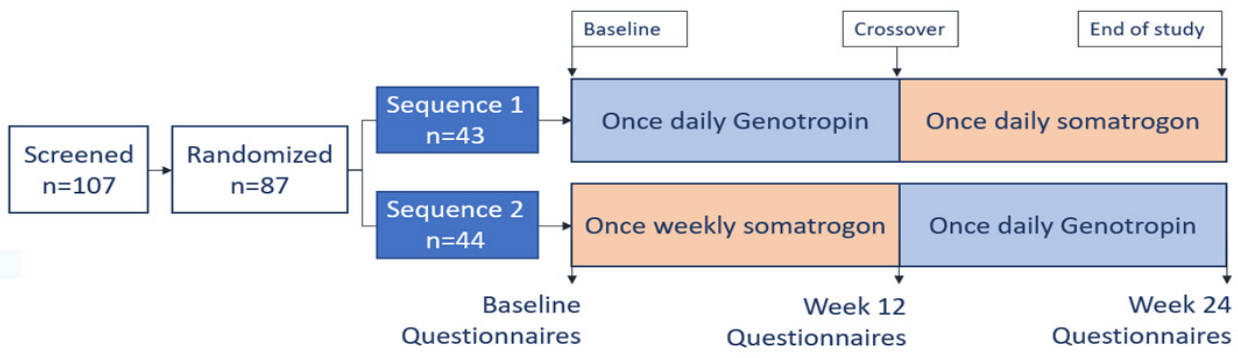
The primary endpoint was treatment burden assessed as the difference in mean overall PLI total scores between weekly and daily injection schedules, completed after each 12-week treatment period.

A post-hoc responder analysis of PLI scores using an anchor-based approach was conducted on patients who completed the patient LI questionnaire at BL, Week 12, and Week 24.

For this analysis, for each injection schedule responders were defined as decrease of ≥ 18 points from Baseline on Overall PLI total score. A non-responder was defined as increase >0 or decrease < 18 points from Baseline on Overall PLI total score.

Given the paired nature of the data, a McNemar's test was used to determine if the proportion of responders for each treatment schedule was significantly different.

Figure 1. Study design and patient flow



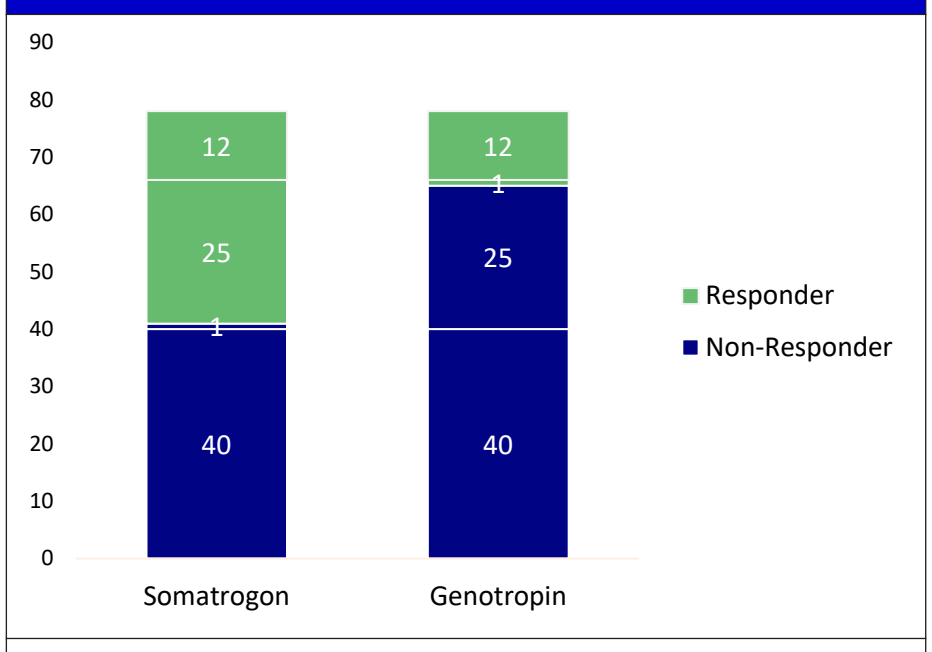
Assessments

- The validated DCOA questionnaire was administered electronically to the Dyad (child & caregiver together). The DCOA includes a robust list of questions to determine the treatment burden. It has 2 parts: DCOA 1 and 2.
- At BL and after each 12-week treatment period, DCOA 1 (rating treatment experience) was completed. After experiencing both treatment schedules, DCOA 2 collected preference data for daily or weekly injections (Fig 1).
- The PLI questionnaire is comprised of 7 items: (interference with) daily activities / social activities / recreation & leisure activities / spending the night away from home / travel / changes to life routine / bother by injections.

Results

- From Feb 2019 to Aug 2020, 87 patients from US, Bulgaria, Czech Republic, Slovakia, and UK were randomized and treated with ≥1 dose of study drug (Figure 1), from which 85 completed the study.
- Of the 87 randomized patients, 78 completed the PLI questionnaire at BL, Week 12 and Week 24 and were included in the responder analysis.
- Using the responder definition, during treatment with:
  - Genotropin : 13 patients (16.7%) were responders and 65 (83.3%) were non-responders (Figure 1).
  - Somatrogon: 37 (47.4%) were responders and 41 (52.6%) were non-responders (Figure 1).
- The proportion of responders is significantly different ($p<0.0001$) between each treatment, in favour of somatrogon.

Figure 1 : Number of Responders and Non-Responders During Somatrogon and Genotropin Treatment Periods



The numbers in the figure represent the counts in the 2x2 contingency table to which McNemar's test was applied. There were 40 patients who were non-responders for both treatment schedules, 12 who were responders for both treatment schedules, 25 who were responders for somatrogon but not for Genotropin, and 1 who was responder for Genotropin but not for Somatrogon.

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