Long-Term Safety of a Once-Weekly Somatrogon (hGH-CTP): 4-Year Results of a Phase 2 Extension Study in Children with Growth Hormone Deficiency

Nataliya Zelinska, Yulia Skorodok, Oleg Malievsky, Violeta Iotova, Ron G. Rosenfeld, Zvi Zadik, Shelly Vander, and Aleksandra Pastrak

1Ukrainian Children Specialized Clinical Hospital, Kyiv; 2St. Petersburg State Pediatric Medical University, St. Petersburg; 3Bauchik State Medical University, Ufa; 4UMHAT, Varna; 5Oregon Health & Science University, Oregon, USA; 6Kaplan Medical Center, Rehovot, Israel; 7OPKO Biologics, Kirkat Gat, Israel; 8OPKO Health, Miami.

BACKGROUND

Once-daily growth hormone (GH) therapy is an effective treatment for children with growth hormone deficiency (GHD), but a decrease in compliance with prolonged treatment can reduce the treatment benefits. Somatrogon, also known as MOD-4023, is a long-acting recombinant protein consisting of human growth hormone (hGH) and three copies of C-terminal peptide (CTP). It is a new molecular entity with receptor binding properties and a mechanism of action analogous to hGH. A once-weekly somatrogon (hGH-CTP), is being developed to reduce the treatment burden of daily dosing for children and caregivers and potentially improve compliance and long-term efficacy [1].

Objective:

The objective of the open-label extension (OLE) Phase 2 study was to demonstrate the long-term impact of once-weekly somatrogon treatment beyond the initial 12 months of the primary study. Key objectives of this report included evaluation of safety, local tolerability, growth outcome and immunogenicity in patients treated with somatrogon for a period of up to 4 years in the OLE.

METHODS

The OLE phase 2 study was a continuation of a randomized 12-month study that investigated the efficacy, safety, and tolerability of 3 dose levels of somatrogon, administered weekly (0.25, 0.48, or 0.66 mg/kg/week) compared to daily r-hGH (Genotropin® 0.034 mg/kg/day) in pre-pubertal pediatric patients with GHD [2].

Forty-eight children with GHD that completed the main Phase 2 study continued with the same dose of somatrogon in the OLE. Subjects who were randomized to somatrogon in the main study continued with ongoing somatrogon therapy. Subjects who were randomized to Genotropin in the main study continued with daily Genotropin (N=15) and those who were assigned to the 12-month Phase 2 study continued with the same dose of somatrogon; subjects who were originally assigned to daily Genotropin® (N=44).

RESULTS: Efficacy

- Mean annualized HV over 3 years in the OLE shows that long-term somatrogon was well-tolerated and maintained long-term normalization over time.
- IGF-1 and IGF-binding protein-3 (IGFBP-3) levels remained within the normal range with ongoing somatrogon therapy.
- Subjects that had developed non-neutralizing Abs demonstrated similar annualized HV (cm/year) to subjects with no detectable Abs (8.43 (1.03) vs. 7.85 (1.66), 7.17 (1.31) vs. 7.19 (1.25), and 6.71 (1.19) vs. 7.36 (1.56)); and height SDS [-2.31 (1.22) vs. -1.98 (0.70), -1.71 (1.10) vs. -1.54 (0.63), and -1.47 (1.12) vs. -1.15 (0.80) for OLE year 1, 2, and 3, respectively).

RESULTS: Demographics at the Start of Open Label Extension

- Mean age (SD), years: 7.65 (2.104) vs. 7.32 (2.667), 45 (83.8) vs. 47 (97.9)
- Pubertal status Tanner I (%): 47 (97.9) vs. 32 (66.7), 45 (83.8) vs. 47 (97.9)
- Race, white (%): 45 (83.8) vs. 32 (66.7)
- Mean height (SD), cm: 122.6 (11.07) vs. 112.6 (11.07)
- Mean BMI (SD), kg/m²: 15.82 (1.740) vs. 15.82 (1.740)
- Mean IGF-1-SDS (SD), Z: 0.03 (1.176) vs. 0.03 (1.176)

RESULTS: OLE Safety Years 1 to 4

- All (N=48) vs. All (N=48): Mean age (SD), years: 7.65 (2.104) vs. 7.32 (2.667), 45 (83.8) vs. 32 (66.7), 45 (83.8) vs. 47 (97.9)
- Mean weight (SD), kg: 20.39 (5.150) vs. 20.39 (5.150), 41 (83.8) vs. 41 (83.8)
- Mean height (SD), cm: 122.6 (11.07) vs. 112.6 (11.07), 41 (83.8) vs. 41 (83.8)
- Mean BMI (SD), kg/m²: 15.82 (1.740) vs. 15.82 (1.740), 38 (78.2) vs. 38 (78.2)
- Mean IGF-1-SDS (SD), Z: 0.03 (1.176) vs. 0.03 (1.176)

CONCLUSION

- Somatrogon treatment demonstrated a favorable safety profile and local tolerability after four years of dosing in GH deficient pediatric subjects.
- Serum IGF-1-SDS values were maintained within the normal range, and a growth rate comparable to that reported for daily hGH was observed.
- Low titers of non-neutralizing Abs did not affect growth parameters and IGF-1 levels.

REFERENCES


This is a partial representation of the document. The full document can be found in PDF format on the preceding page.