*Updated: 7/31/2023*

# New Drugs and Therapeutics Update

## NGENLA™ (Somatrogon-ghla)

On June 27, 2023, the U.S. Food and Drug administration approved NGENLA (somatrogon-ghla), a once-weekly, human growth hormone analog indicated for treatment of pediatric patients aged three years and older with growth failure due to growth hormone deficiency (GHD). NGENLA is now available for U.S. prescribing.

Somatrogon is a long-acting rhGH that contains the amino acid sequence of hGH and 3 copies of the C-terminal peptide (CTP) of the β-chain of human chorionic gonadotropin (2).

A multicenter, open-label, randomized phase 2 study in prepubertal, growth hormone naive children with **GHD (isolated or as part of multiple pituitary hormone deficiency)** compared the safety, tolerability, and efficacy of 3 different doses of somatrogon (0.25, 0.48, and 0.66 mg/kg/week) administered once weekly vs rhGH (somatropin (Genotropin); 0.24 mg/kg/week) administered once daily (3). Children with cancer or chemotherapy/radiation therapy exposure, children with chromosomal abnormalities, history of small for gestational age, poorly-controlled diabetes mellitus, or BMI ≤ - 2SDS were excluded. The estimated half-life of somatrogon administered once weekly was 18 to 36 hours, which was ~5- to 10-fold longer than that of somatropin (3,4). Subjects in all 3 somatrogon dose cohorts showed acceleration of growth velocity following 12 months of treatment and a dose dependent increase in growth factor levels. During the study, doses of somatrogon and somatropin were adjusted based on body weight and according to a predefined dose-adjustment algorithm to guide dose decrease in case of high IGF-1 levels. The IGF-I SDS values remained ≤ 2 SDS in all of the study drug cohorts, with the exception of one subject in the 0.66 mg/kg/week somatrogon group who experienced mild elevation in IGF-1 SDS between 2 to 2.5SDS, which persisted after dose reduction to 0.48 mg/kg/week. The phase 2 data indicated that the somatrogon dose of 0.66 mg/kg/week elicited a comparable response outcome [height velocity (HV) SDS and height SDS at 12 months] to daily somatropin administration. Somatrogon demonstrated an acceptable safety profile during treatment with no serious adverse events (SAEs) and no discontinuations due to adverse events (AEs) associated with somatrogon or somatropin. Additionally, the incidence of development of anti-drug antibodies was similar for the study drug and the control group and no anti-CTP antibodies were observed. The tolerability of treatment with once weekly somatrogon was similar to that of somatropin (3,4). IGF-1 obtained 4 days (96 hours) after somatrogon dosing was the best indicator of mean IGF-1 levels throughout the week (4,5).

Based on the dose findings of the phase 2 trial, a 12-month, open-label, multicenter, randomized, active-controlled, parallel-group, phase 3 study was conducted as a noninferiority study comparing somatrogon 0.66 mg/kg/week once weekly dose to somatropin administered once daily (0.24 mg/kg/week) in prepubertal children with GHD. The study demonstrated noninferiority of once-weekly somatrogon vs daily somatropin for the primary endpoint of 12-month height velocity (10.10 cm/yr vs 9.78 cm/yr, respectively) and concluded that long-acting somatrogon and daily GH had similar safety and tolerability profiles with the added benefit of less-frequent injection schedule afforded by somatrogon (6,7).

*Updated: 7/31/2023*

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