Design and Clinical Development of TransCon Growth Hormone for Growth Hormone Deficiency

Michael Becker1, Jan Møller Mikkelsen2, Grethe Noerskov Rasmussen1, Hailard Rau3, Kenneth Sprogøe4, Jonathan A Leff, MD5
1Ascendis Pharma A/S, 2Ascendis Pharma Inc, 3Ascendis Pharma GmbH

This study was sponsored by Ascendis Pharma A/S.

Background

TransCon Growth Hormone is designed as a once-weekly sustained-release prodrug of recombinant human growth hormone (hGH, somatropin). In its produg form, hGH is transiently bound to the TransCon carrier via the TransCon linker. Through auto-hydrolysis, unmodified native GH is released with a Chemical and AUC comparable to daily therapy. TransCon Growth Hormone leverages the known pharmacology of daily hGH and is being developed for the treatment of Growth Hormone Deficiency (GHD) in children and adults.

Healthy adults (n=68) were included in two Phase 1 single-dose pharmacokinetic (PK) and pharmacodynamics (PD) studies investigating TransCon hGH (0.04 mg to 0.36 mg hGH/kg/week).

Results – Two Phase 1 Studies

TransCon hGH: • Was safe and well tolerated, • Suitable for a once-weekly dosing regimen, • Provided a hGH (PK) and IGF-1 (PD) response comparable to daily hGH throughout the dosing period.

Methods

TransCon Growth Hormone was investigated in two Phase 1 studies of healthy volunteers and two Phase 2 studies in adults and children with GHD. Dose-equivalent daily hGH was included in most of the studies to compare GHD-levels, IGF-1 levels, and height velocity.

The TransCon hGH produg consists of hGH transiently bound to a polyethylene glycol carrier via a TransCon linker. Released hGH is completely and designed to maintain the same mode of action and distribution in the body as endogenous hGH.

TransCon hGH, stored at room temperature, can be administered in small volumes with a fine (31G) needle at comparable weekly dose-levels to daily hGH.

Results – Phase 2 Adult GHD Study

In a Phase 2 study of subjects with Adult Growth Hormone Deficiency (AGHD) (n=37) administered repeat dosings, TransCon hGH demonstrated dose-linearity over a range of 0.02 to 0.08 mg v/h/week, and comparable efficacy (IGF-1) to the dose-equivalent daily hGH control group (0.04 mg hGH/kg/week).

Results – Phase 2 Pediatric GHD Study

A Phase 2 study of pediatric patients with GHD (n=53) confirmed the safety, tolerability, and suitability of TransCon hGH for once-weekly dosing. A TransCon hGH equivalent dose to daily hGH demonstrated slightly higher growth rates.

Conclusions

To date, TransCon Growth Hormone has demonstrated efficacy and safety comparable to that observed with daily hGH:

- Injection site reactions were generally mild and similar to daily hGH injections, with no nodule formation or lipatrophy noted.
- No neutralizing anti-hGH antibodies occurred.
- TransCon hGH was shown to be dose-linear across different dose-levels (hGH and IGF-1).
- TransCon hGH demonstrated the same therapeutic effect (annualized height velocity) to daily hGH at the same weekly dose-level (pediatric GHD study: 0.21 mg hGH/kg/week).
- TransCon hGH can be administered in small volumes with a fine (31G) needle at comparable weekly dose-levels to daily hGH.
- The completed Phase 1 and 2 studies supported the initiation of the hGH Trial – A Phase 3 study in pediatric GHD.

References: