A Phase 2, six-month, randomized, active-controlled, safety and efficacy study of TransCon hGH compared to daily hGH in children with Growth Hormone Deficiency (GHD)

Pierre Chatelain[1], MD; Oleg Malievsky[2], MD; Klaudziya Radziuk[3], MD; Ganna Senatorova[4], MD; Michael Beckert[5], MD

[1]University Claude Bernard, Lyon, France, [2]Bashkir State Medical University, Ufa, Russia, [3] 2nd Children City Clinic, Minsk, Belarus, [4]Kharkiv National Medical University, Kharkiv, Ukraine, [5]Ascendis Pharma A/S, on behalf of the TransCon hGH study group

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Background

TransCon hGH is a long-acting prodrug of recombinant human Growth Hormone (rhGH) that releases fully active unmodified rhGH into the blood compartment. In Phase 1 and Phase 2 AGHD studies, TransCon hGH was shown to:

1) Be safe and well tolerated,
2) Be suitable for a once-weekly dosing regimen,
3) Provide a pharmacokinetic (PK) hGH and pharmacodynamic (PD) IGF-I response comparable to daily hGH treatment throughout the dosing period.

This pediatric Phase 2 clinical study was designed to investigate the safety, efficacy, pharmacokinetics and pharmacodynamics of TransCon hGH compared to daily hGH over a treatment period of six months. Topline data of the full analysis set are reported in this poster.

Figure 1: The TransCon hGH prodrug consists of hGH transiently bound to a polyethylene glycol carrier molecule via a TransCon linker. The released hGH is unmodified, and designed to maintain the same mode of action and distribution in the body as daily hGH.

Objectives

The objective of this study is to investigate

1) Safety and Tolerability,
2) Pharmacokinetics and Pharmacodynamics,
3) Efficacy of TransCon hGH

in children with Growth Hormone Deficiency.

Design and Methods

Pre-pubertal, treatment naïve GHD children received s.c. injections of one of three once-weekly TransCon hGH doses (0.14, 0.21 and 0.30 mg rhGH/kg/week) or daily hGH (Genotropin®; 0.03 mg rhGH/kg/day = 0.21 mg rhGH/kg/week) over a six-month treatment period, in a randomized Phase 2 study. GHD diagnoses were established in accordance with international consensus guidelines.

Demographics

Mean + SD	All subjects	0.14 mg rhGH/ kg/week TransCon hGH	0.21 mg rhGH/ kg/week TransCon hGH	0.30 mg rhGH/ kg/week TransCon hGH	0.03 mg rhGH/ kg/day Genotropin®
# Subjects	53	12	14	14	13
Age (years) Baseline	8.0 (2.5)	8.2 (2.9)	8.4 (2.1)	7.5 (2.8)	7.7 (2.5)
Height SDS	-3.1 (0.9)	-3.1 (1.1)	-2.8 (0.4)	-3.2 (1.0)	-3.3 (1.1)
GH Stimulation Test * [ng/mL] (Screening)	5.0 (2.8)	5.1 (3.2)	5.2 (2.6)	4.4 (2.8)	5.2 (3.1)
IGF-I SDS	-2.2 (0.8)	-2.0 (0.7)	-2.0 (0.8)	-2.2 (0.7)	-2.5 (0.9)

* The higher peak of the two performed GH stimulation tests was used for calculation of the mean.

Results - Growth

Annualized height velocities among the three once-weekly TransCon hGH doses ranged from 11.9 cm for the 0.14 mg rhGH/kg/week dose to 13.9 cm for the 0.30 mg rhGH/kg/week dose, which were comparable to 11.6 cm for the active comparator, daily injections of Genotropin® at a cumulated dose of 0.21 mg rhGH/kg/week.

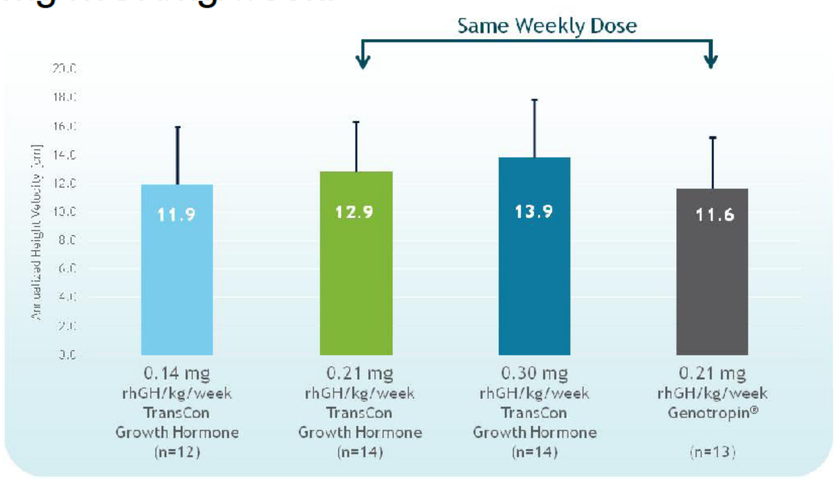

Figure 2: Annualized Height Velocity (Mean + SD) of full dataset of 53 patients after 6 months of treatment.

Results - PK/PD

A full PK/PD profile was established in week 13. Maximum hGH blood concentration is comparable between equivalent weekly doses of TransCon Growth Hormone and daily hGH (Figure 3). IGF-I levels (SDS) increased dose-proportionally and was normalized for all dose groups (Figure 4) following dosing of the three TransCon Growth Hormone dose levels.

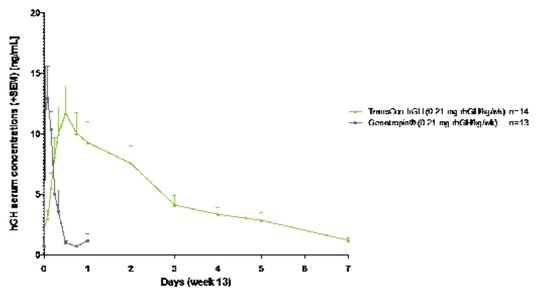

Figure 3: hGH levels for TransCon hGH (0.21 mg rhGH/kg/week) and daily hGH (0.21 mg rhGH/kg/week).

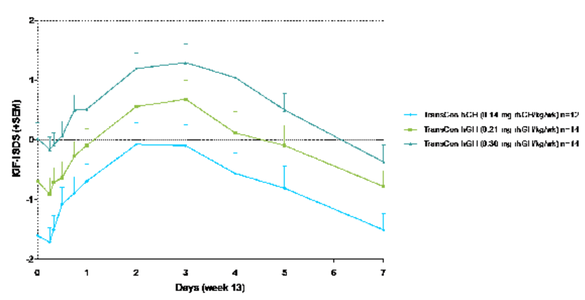

Figure 4: IGF-I SDS levels increased dose-proportionally and was normalized for all dosing groups following dosing of the three TransCon hGH dose levels.

Safety

No safety concerns were observed. Injection site reactions have generally been mild and similar to what is expected with daily hGH injections, with no nodule formation or lipoatrophy noted.

Conclusion

The results of this Phase 2 study in pediatric patients with GHD confirms the safety, tolerability and the suitability of TransCon hGH for once-weekly dosing. An equivalent dose-level to daily hGH demonstrated numerically higher growth rates compared to daily hGH treatment. No drug-related SAEs occurred, no lipoatrophy or nodule formation was seen. IGF-I changes suggest a dose response and levels are in the expected range.

Participating Investigators:
M. Omar Abdou, MD; M. Aryayev, MD; G. Balazs, MD; P. Barat, MD; T. Battelino, MD; I. Ben-Skowronek, MD; E. V. Bolshova, MD; P. Chatelain, MD; S. Darcan, MD; H. Hassan Elsedfy, MD; E. Erhardt, MD; C. Georgescu, MD; M. Mamdouh Hassan, MD; V. Iotova, MD; S. Koloušková, MD; O. Malievskiy, MD; O. Marginean, MD; A. Mazur, MD; E. Mikhailova, MD; V. Mogos, MD; K. Mohnike, MD; A. Muzsnai, MD; I. Pascanu, MD; V. Peretyatko, MD; V. Peterkova, MD; R. Pfäffle, MD; G. Senatorova, MD; A. El Sharkawy, MD; Z. Siklar, MD; J. Skorodok, MD; J. Škvor, MD; M. Szalecki, MD; K. Radziuk, MD; Z. Vajda, MD; E. Vlachopapadopolou, MD; J. Weill, MD; N. Zelinska, MD; K. Ziora, MD

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Pierre Chatalain
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