Six-Month Interim Safety and Efficacy of Different Dose Levels of TransCon hGH Administered Once-weekly Versus Standard Daily Human Growth Hormone Replacement Therapy in Pre-Pubertal Children with Growth Hormone Deficiency (GHD)

Pierre Chatelain[1], MD, Oleg Malievsky[2], MD, Klaudziya Radziuk[3], MD,
Heba Hassan Elsedfy[4], MD, Evgenia Mikhailova[5], MD, Michael Beckert[6], MD

[1]University Claude Bernard, Lyon, France, [2]Bashkir State Medical University, Ufa, Russia, [3] 2nd Children City Clinic, Minsk, Belarus,
[4]Ain Shams University Hospital, Cairo, Egypt, [5]Samara State Medical University, Samara, Russia, [6]Ascendis Pharma A/S, on behalf of the TransCon hGH study group

Background

TransCon hGH is a long-acting prodrug of recombinant human Growth Hormone (hGH) that releases fully active unmodified hGH into the blood compartment. TransCon hGH was shown in two Phase 1 studies in Healthy Volunteers and a Phase 2 study in adults with GH Deficiency (AGHD) to:

1) Be safe and well tolerated,
2) Produce dose dependent, predictable levels of growth hormone,
3) Be suitable for a once-weekly dosing regimen,
4) Provide a pharmacokinetic (PK) hGH and IGF-I pharmacodynamic (PD) response comparable to daily hGH throughout the dosing period.

This interim analysis consists of 25 patients (approximately 50 % of the total enrollment in the study) completing all six months of treatment, and demonstrates that TransCon hGH has a safety and efficacy profile comparable to daily hGH.

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 unmodifed, 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 hGH/kg/week) or daily hGH (Genotropin®; 0.03 mg hGH/kg/day = 0.21 mg/kg/week) over a six-month treatment period, in a randomized, comparator-controlled dose response Phase 2 study. Patient GHD diagnoses were established in accordance with international consensus guidelines, based on auxology (height & height velocity), GH stimulation tests & IGF-I. Children Small for Gestational Age (SGA) were excluded.

Demographics

Mean + SD	All subjects	0.14 mg/ kg/week TransCon hGH	0.21 mg/ kg/week TransCon hGH	0.30 mg/ kg/week TransCon hGH	0.03 mg/ kg/day Genotropin
# Subjects	25	6	6	7	6
Age (Screening; years)	7.39 (2.25)	7.62 (2.51)	7.29 (2.29)	7.08 (2.68)	7.61 (1.94)
Height SDS	-3.22 (1.02)	-3.23 (1.48)	-2.85 (0.47)	-3.12 (0.72)	-3.71 (1.22)
GH Stimulation Test [ng/mL] (Screening)	4.50 (2.91)	4.38 (3.03)	5.54 (2.62)	3.34 (2.57)	4.95 (3.62)
IGF-I SDS	-2.43 (0.78)	-2.27 (0.69)	-2.29 (0.72)	-2.41 (0.78)	-2.77 (1.00)

Results: Growth

At 6 months (Figure 2B), mean annualized height velocities among the three dosing levels administered weekly ranged from 11.9 cm for the 0.14 mg/kg/week dose to 14.5 cm for the 0.30 mg/kg/week dose, which were comparable to 11.5 cm for the active comparator, daily injections of Genotropin® at a 0.21 mg/kg/week dose.

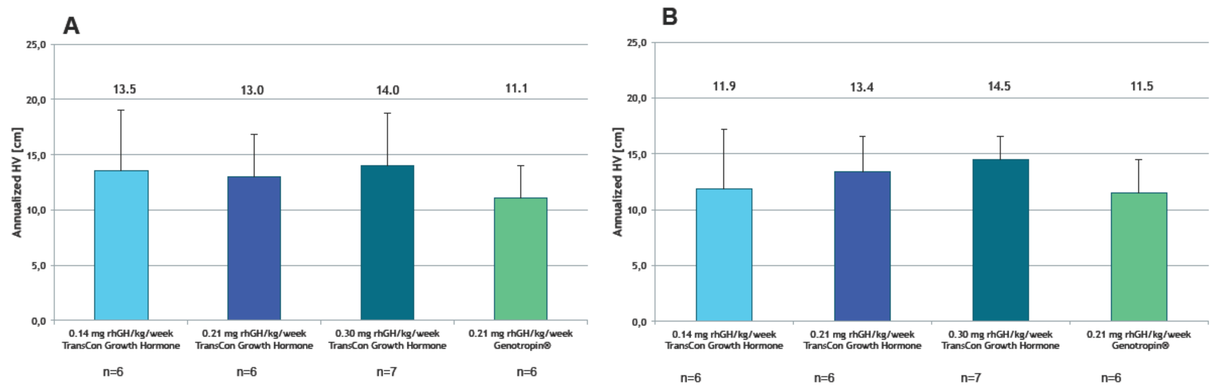

Figure 2: Mean annualized Height Velocity at 3 months (A) and 6 months (B)

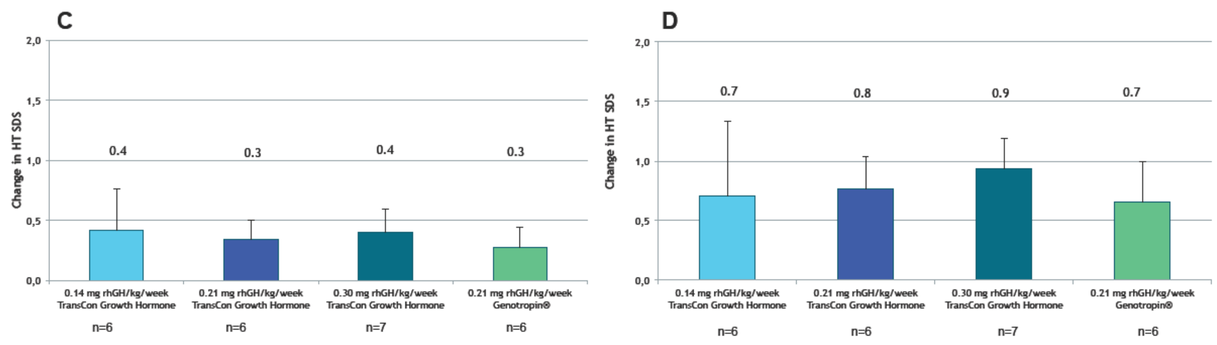

Figure 3: Mean change in HT SDS from baseline to 3 months (C) and 6 months (D)

Results: PK/PD

Maximum hGH blood concentration is comparable between equivalent weekly doses of TransCon Growth Hormone and daily hGH (Figure 4); and a dose-proportional increase in IGF-I levels (SDS) into the normal range (Figure 5) was observed following dosing of the three TransCon Growth Hormone dose levels.

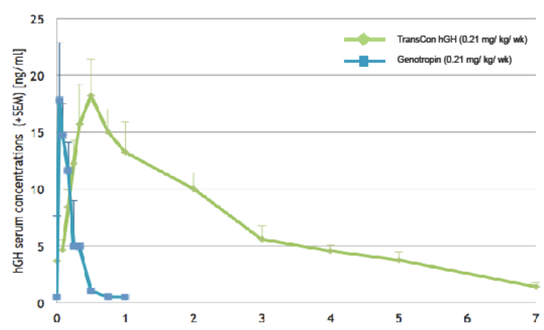

Figure 4: hGH levels for TransCon hGH (0.21 mg rhGH/kg/week) and daily hGH (0.21 mg rhGH/kg/week)

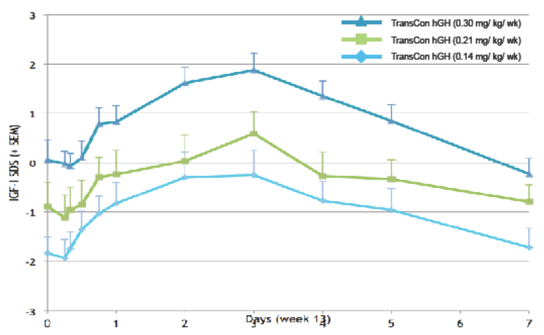

Figure 5: Dose proportional IGF-I SDS elevation into the Normal range following dosing of the three TransCon Growth Hormone dose levels

Conclusion

To date, TransCon hGH has demonstrated efficacy and safety comparable to that observed with daily hGH. Injection site reactions have generally been mild and similar to what is expected with daily hGH injections, with no nodule formation or lipoatrophy noted. This TransCon hGH Phase 2 study conducted in a pediatric population confirms the excellent safety and efficacy profile observed in previous clinical trials.

17 ECE 120--EP
Steroids, developmental and paediatric endocrinology
Michael Beckert
DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY
PosterSessionOnline.com