12-Month effects of once-weekly and twice monthly Administration of hybrid Fc-fused human growth hormone, GX-H9, treatment in pediatric patients with GHD

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Introduction

Recombinant human growth hormone (rhGH) is a standard treatment for children with growth hormone deficiency (GHD). However, current rhGH therapy involves daily subcutaneous injections with years of therapy. The challenge of daily rhGH injections has proven to limit compliance, often reducing the ability to maintain height velocity (HV) or optimal clinical outcomes. Thus, long-acting rhGH could improve ease of compliance, and real-world efficacy.

Objectives

GX-H9 is a long-acting form of recombinant human GH under clinical development for both adults and children with GH deficiency (GHD). This study was designed to compare 12-month effects of once-weekly and twice-monthly (every other week; EOW) administration of GX-H9 treatment to that of daily GH, Genotropin®,* in pediatric patients with GHD.

Methods

A Phase 2, randomized, open-label, active-controlled, parallel, dose finding study of GX-H9 is being conducted at 27 endocrinology centers in 10 countries (Europe, Middle East and Republic of Korea) for pre-pubertal treatment-naïve children with GHD. (EudraCT Number: 2015-001939-21, ClinicalTrials.gov Identifier: NCT03309891)

Subject Disposition and Characteristics

• 56 subjects were randomized and 2 out of 56 subjects withdrew before dosing. Afterward, 4 subjects dropped out during multiple dose period.
• A total of 50 subjects completed 12 months of treatment.

Table 1. Demographic and Baseline Characteristics (N=54)

<table>
<thead>
<tr>
<th>0.8 mg/kg/weekly</th>
<th>1.2 mg/kg/weekly</th>
<th>2.4 mg/kg/weekly</th>
<th>0.05 mg/kg/EOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>GX-H9</td>
<td>Genotropin®</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Age (years), mean (SD)</td>
<td>6.85 (2.28)</td>
<td>6.70 (2.03)</td>
<td>6.97 (2.61)</td>
</tr>
<tr>
<td>Gender (Male/Female), n (%)</td>
<td>25 (51.74)</td>
<td>11 (18.62)</td>
<td>12 (92.31)</td>
</tr>
<tr>
<td>Race (Caucasian/Asian), n (%)</td>
<td>12 (21.17)</td>
<td>11 (18.62)</td>
<td>12 (92.31)</td>
</tr>
<tr>
<td>BMI SDS, mean (SD)</td>
<td>0.66 (1.37)</td>
<td>0.32 (1.09)</td>
<td>0.19 (0.92)</td>
</tr>
<tr>
<td>Height SDS, mean (SD)</td>
<td>-3.66 (1.05)</td>
<td>-3.43 (0.61)</td>
<td>-3.09 (0.62)</td>
</tr>
<tr>
<td>aHV SDS, mean (SD)</td>
<td>-1.99 (1.85)</td>
<td>-3.43 (1.87)</td>
<td>-1.85 (1.08)</td>
</tr>
<tr>
<td>IGF-1 SDS, mean (SD)</td>
<td>-2.49 (1.14)</td>
<td>-2.22 (1.15)</td>
<td>-2.37 (1.15)</td>
</tr>
<tr>
<td>Stimulated Growth Hormone (ng/mL), mean (SD)</td>
<td>5.12 (3.50)</td>
<td>4.61 (2.83)</td>
<td>4.49 (3.15)</td>
</tr>
<tr>
<td>Peak GH concentration during stimulation test (µg/mL), n (%)</td>
<td>7 (50.00)</td>
<td>5 (38.46)</td>
<td>6 (46.15)</td>
</tr>
</tbody>
</table>

Results – Safety (12 months)

• All treatment-emergent adverse drug reactions were mild to moderate and mostly transient.
• No hypotension, injection site nodule formation or insulin resistance was observed.

Results – Efficacy (12 months)

The height velocity at 12 months indicated comparable growth rate between all doses of GX-H9 (both weekly and EOW schedules) and the active comparator, Genotropin®.

Figure 3. Mean (SD) annualized height velocity at 6 months and 12 months after treatment.

Changes in height SDS from baseline to 6 months and 12 months of treatment were comparable between all doses of GX-H9 (both weekly and EOW schedules) and the active comparator, Genotropin®.

Figure 4. Mean (SD) height SDS at baseline, 6 months and 12 months after treatment.

Average peak IGF-1 SDS were within range of -2 SDS to +2 SDS for 12 months in subjects with all doses of GX-H9 (both weekly and EOW treatment) and the active comparator, Genotropin®.

Figure 6. Mean (SD) peak IGF-1 SDS throughout 12 months of treatment.

Conclusions

• Height velocity and Height SDS at 12 months were comparable across GX-H9 treatment groups and the active comparator Genotropin® group.
• GX-H9 treatment for 12 months was safe and well-tolerated as Genotropin®, for GH-naïve patients with PGHD.
• GX-H9 showed potential for both weekly and twice-monthly administration in children with GHD.

ACKNOWLEDGMENTS: This study was sponsored by Genexine, Inc. and Handok Inc. This research was supported by Korea Drug Development Fund (KDFD) funded by MSIP, MOTIE and MOH(W) (Grant No. KDFD-2015308-07 for Phase I Study, KDFD-2015302-11 for Phase II AGHD Study, & KDFD-2015309-12 for Phase II PGHD Study).

DISCLOSURE: SY Lee is an employee and shareholder of HANDOK Inc. Ji Choi, Ji Ji, J Woo, Y C Sung are employees and stockholders of Genexine, Inc.

* Genotropin® 0.03 mg/kg/daily: seven doses on seven consecutive days during single dose PK/PD period.

Figure 2. Overall Study Design

Figure 1. Structure of GX-H9.

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