Once-Weekly Administration of Sustained-Release Rhgh in Prepubertal Children with Idiopathic Short Stature: Phase II Dose Finding Study

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Body

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Background Idiopathic short stature (ISS) is a heterogeneous group of stunted growth conditions with unknown etiology. For a treatment of ISS, recombinant human growth hormone (rhGH) has been approved since 2003, and many studies confirmed its efficacy and safety. LB03002 is a once-weekly sustained-release formulation of rhGH and its efficacy and safety were already confirmed in children and adults with GH deficiency. In this study, the efficacy and safety of LB03002 was compared with daily rhGH in children with ISS, and the optimal dose of LB03002 for a phase III confirmatory study was determined.

Design and methods

This was a phase II, multicenter, randomized, active-controlled, open-label study. Forty-six prepubertal and treatment-naïve ISS children were received subcutaneous injections of one of LB03002 doses (0.5 (n=14) and 0.7 mg/kg/week (n=16)) or daily rhGH (0.37 mg/kg/week (n=16)) for 26 weeks. The change in height velocity (HV) from baseline, auxological assessments, blood hGH concentration, and serum levels of insulin-like growth factor-I (IGF-I) and insulin-like growth factor binding protein-3 (IGFBP-3) were evaluated during 26-week treatment period. The safety profiles were also assessed.

Results

All patients were at Tanner stage 1, and all groups were well balanced in the demographic and clinical characteristics. LB03002 at both doses as well as daily rhGH resulted in significant increases of HV in children with ISS. At Week 26, no statistical significant difference was found in the actual mean HV changes between each of LB03002 groups and control group. In the analysis of covariance for HV, the least square means of HV change (cm/year) at Week 26 were 5.08 with control group, 3.65 and 4.38 with LB03002 groups of low dose and high dose,

respectively. The change in height SDS of LB03002 high dose group at Week 26 was similar with that of control group. Both LB03002 groups showed significant increase in hGH level, which was dose dependent, and serum IGF-I and IGFBP-3 levels at Week 26 increased significantly from baseline without no statistical difference between groups. The observed adverse events were generally mild and short-lived. Anti-hGH was detected from 9/30 (30%) patients in LB03002 groups at Week 26 without significant effect on HV or blood hGH concentration.

Conclusions:

Once weekly regimen of LB03002 at 0.7 mg/kg/week demonstrated the comparable efficacy profiles to daily rhGH 0.37 mg/kg/week in terms of increases in HV and height SDS as well as normalization of IGF-I and IGFBP-3. LB03002 was well tolerated, and its safety profile was comparable with daily rhGH. According to this study, once weekly LB03002 0.7 mg/kg/week is recommended as the optimal dose of LB03002 for a phase III confirmatory study in children with ISS.

Disclosure: JSH: Committee Member, LG Life Sciences, Ltd.. KHL: Committee Member, LG Life Sciences, Ltd.. HWY: Committee Member, LG Life Sciences, Ltd.. BKS: Committee Member, LG Life Sciences, Ltd.. CHS: Committee Member, LG Life Sciences, Ltd., Board Member, LG Life Sciences, Ltd.. HSH: Committee Member, LG Life Sciences, Ltd.. SH: Employee, LG Life Sciences, Ltd.. JYS: Employee, LG Life Sciences, Ltd.. HSK: Committee Member, LG Life Sciences, Ltd.. Nothing to Disclose: HSL, DYL, CWK, WYC, DKJ

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