SAT-091

Somapacitan is a long-acting, reversible albumin-binding growth hormone (GH) derivative being developed for once-weekly dosing in adults and children with GH deficiency (GHD). The efficacy, safety and tolerability of somapacitan were compared with daily GH in children with GHD in a multicenter, randomized, controlled, double-blinded to dose, phase 2 trial (REAL 3, NCT02616562). Treatment-naïve, prepubertal children with GHD were randomized 1:1:1:1 to once-weekly sc somapacitan (0.04, 0.08 or 0.16 mg/kg/week [wk]) or daily sc GH (Norditropin®; 0.034 mg/kg/day) during the 26-wk main trial period and 26-wk extension. Efficacy of the 0.16 mg/kg/wk dose was similar to that of daily GH, judged by height standard deviation scores (SDS) and insulin-like growth factor-I SDS, and, at wk 52, height velocity was statistically significantly greater with somapacitan 0.16 mg/kg/wk vs daily GH. Safety and tolerability of somapacitan were consistent with the profile of daily GH. Here, we report the results of a pre-planned analysis of patient-reported outcomes (PROs) collected during REAL 3. This is, to our knowledge, the first report of a disease-specific PRO score from a randomized trial in GHD. PROs were investigated using the Growth Hormone Deficiency - Child Impact Measure observer-report (GHD-CIM ObsRO). This is a new, validated questionnaire, developed according to US FDA guidance, to assess the impact of GHD on physical functioning, and social and emotional wellbeing in children aged 4 to <13 years, to be completed by caregivers. Minimal important differences (MID) in scores were determined based on Patient and Clinician Global Impression of Severity. Changes from baseline to wk 52 in GHD-CIM ObsRO scores were compared between daily GH and each dose of somapacitan, and were analyzed using an analysis of covariance model.

A total of 59 patients were randomized (somapacitan n=45; daily GH n=14); the full analysis set included 57 children (somapacitan: 0.04 mg/kg/wk n=14; 0.08 mg/kg/wk n=15; 0.16 mg/kg/wk n=14; daily GH n=14). Mean age was 5.9 years; 60% were male; 11 children were <4 years old at baseline. For the change from baseline in GHD-CIM ObsRO score, the estimated treatment differences (ETDs) between somapacitan 0.16 mg/kg/wk and daily GH at wk 52 exceeded the MID in favor of somapacitan for the emotional wellbeing (ETD -9.34; MID 7) and social wellbeing domains (ETD -10.12; MID 5), as well as total score (ETD -7.43; MID 5). The somapacitan 0.16 mg/kg/wk group showed a numerical improvement over daily GH across all GHD-CIM ObsRO domains and total score, although none of the ETDs reached statistical significance.

At 52 wks, the difference in GHD-CIM ObsRO scores between somapacitan 0.16 mg/kg/wk and daily GH exceeded the MID for the total score, and for the emotional and social wellbeing domains, suggesting clinically relevant improvement for these parameters in favor of somapacitan in children with GHD.

Neuroendocrinology and Pituitary

NEUROENDOCRINE & PITUITARY PATHOLOGIES

Adrenal Reserve Testing with the Glucagon Stimulation Test (GST) and Cosyntropin Stimulation Test (CST) in Deployed Veterans with Mild Traumatic Brain Injury

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SUN-311

Introduction: Mild Traumatic Brain Injury (mTBI) is associated with anterior pituitary hormone dysfunction. The potential long-term effect of this injury on pituitary function in Veterans is not clear. We reviewed the utility of the fixed dose Glucagon Stimulation Test (GST) compared with the high dose Cosyntropin Stimulation test (CST) for hypothalamic-pituitary-adrenal (HPA) reserve over time in these patients with mTBI.

Methods: We present an interim report of our 4-year longitudinal prospective pilot study of pituitary function in Veterans diagnosed with mTBI. Of the 34 mTBI Veterans enrolled, we have tested 28 of them (4 female, 24 male; age and BMI, 31.5±7.0 years and 30.4±6.2, mean±SD, respectively) for baseline pituitary hormone levels and cortisol response to the CST. In 22 subjects growth hormone and cortisol responses to GST were tested at baseline (Year 0). Follow-up testing was done for 18 mTBI subjects in Year 1, 13 subjects in Year 2, 10 subjects in Year 3 and 5 subjects in Year 4. The same baseline data were obtained for 14 age-, sex-, deployment- and BMI-matched control subjects without mTBI (2 female,12 male; age and BMI 34.4±6.8 years and 30.5±4.9, mean±SD, respectively). Cortisol cutoffs of <18 mcg/dL with the CST and <9.0 mcg/dL with the GST were used for the diagnosis of adrenal insufficiency.

Results: Secondary adrenal insufficiency (AI), likely partial, was identified during this study on 6 occasions: 3/22 subjects at Year 0, 1/18 at Year 1, 0/13 at Year 2, 1/10 at Year 3 and 1/5 at Year 4. Two baseline subjects with AI reverted to normal in Years 1-3, one relapsed in Year 4 and a third had no further testing. Correlations of the cortisol levels from GST vs the 60-minute cortisol from CST were significant at Year 0 (n=22, r=0.553, p=0.008) and at Year 1 (n=18, r=0.802, p<0.0001). Due to decreased numbers, there were no significant correlations at Years 2 through 4. Similar correlations were obtained using the 30-minute CST values. However, the CST cortisol value predicted the low GST value in only 2/6 subjects. The mean GST cortisol levels and 60-minute CST cortisol levels for subjects at each year were not significantly different over Years 0 through 4 based on ANOVA analyses (CST: F=1.519, p= 0.206; GST: F= 0.796, p=0.532).

Conclusions: Secondary adrenal insufficiency, likely partial, related to mTBI was detected by GST on 6 occasions (twice in one patient) over 4 years of observation. GST can provide useful information about HPA axis reserve, and appears to be more reliable than CST. Identification of potential secondary adrenal insufficiency using the GST in Veterans with mTBI can provide a beneficial combined test for these patients when other testing is not feasible.

Neuroendocrinology and Pituitary

NEUROENDOCRINOLOGY AND PITUITARY

Once-Weekly Somapacitan in Japanese Adults with GH Deficiency Was Well Tolerated, with Similar Efficacy to Daily GH: A Randomized Trial

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