composition are an objective and sensitive endpoint that reflects biologic activity of GH and clinical efficacy of GH replacement.

Methods: The primary objective of the foresiGHt trial is to evaluate the efficacy of once-weekly lonapegsomatropin compared to placebo at 38 weeks in adults with GHD. The trial will be conducted at approximately 120 sites in North America, Europe, Asia, and Oceania. Approximately 240 subjects will be randomized 1:1:1 to once-weekly lonapegsomatropin, once-weekly placebo, or daily somatropin (Norditropin®). Subjects will be treatment-naïve or without GH therapy for at least 12 months. Subjects with well-controlled non-insulin dependent diabetes mellitus (HbA1c ≤ 7.5%) will be eligible. Following screening, the 38-week treatment period will consist of a 12-week gradual dose titration period and 26 weeks of fixed dose maintenance. Fixed dosing will be used to ensure maximal comparability across the treatment arms in the trial. Three dosing groups per arm will be established to allow for differences in age and oral estrogen intake in women.

The primary endpoint is change from baseline in trunk percent fat at week 38, as measured by dual energy X-ray absorptiometry (DXA). Secondary efficacy endpoints are change from baseline in trunk fat mass and change in total body lean mass at week 38. Exploratory efficacy endpoints include total body fat mass, trunk lean mass, visceral adipose tissue, and patient-reported outcomes.

Conclusion: The ongoing global phase 3 foresiGHt trial is designed to assess the efficacy, safety, and tolerability of lonapegsomatropin by weekly administration, compared to weekly placebo and daily hGH replacement therapy in adults with GHD.

Neuroendocrinology and Pituitary

CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Growth Hormone Secretion Does Not Increase After Interleukin-2 Administration in Healthy Men

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Context: Interleukin-2 (IL2), a proinflammatory cytokine, is used for treatment of malignancies. Increased cortisol and ACTH were noted, but GH secretion was not investigated in detail. This is the first study in healthy men which uses moderate high IL2 doses as used in cancer treatment. **Objective:** The goal of this study was to quantify GH secretion after a single sc injection of IL2 in young and older healthy men in relation to dose, age and body composition. **Design:** This was a placebo-controlled, blinded, prospectively randomized cross-over study in 17 young subjects (mean age 24.1 yr) and 18 older subjects (mean age 63.9 yr). The subjects underwent 24 h of blood sampling at 10-min intervals, starting at 1800 h. At 2000 h IL2 (3 or 6 million units per m^2 body surface) or saline was injected sc. Lights were off between 2300 and 0700 h. **Outcome Measures:** Deconvolution analysis of GH. Abdominal visceral fat (AVF) was calculated from single slice CT. **Results:** GH secretion (pulsatile and total) was negatively related to AVF (R=0.67, P<0.0001) and to age (R=0.56, P=0.001). These relations were maintained after IL2 administration. GH profiles were pulsatile under both experimental conditions. Since the effect of IL2 might be limited in time, GH deconvolution analyses were performed on the complete 24 h data series, the period with lights off and 6 h after IL2 administration. Total 24 h GH secretion decreased non-significantly from 74.6 ±10.2 to 67.5±7.4 μg/L (P=0.25) and pulsatile secretion from 69.4±9.8 to 62.2±7.4 μg/L (P=0.23). In the GLM procedure the effect of IL2 treatment was borderline significant (P=0.08), no interaction with age (P=0.28), but borderline with IL2 dose (P=0.07), and caused by decreased GH secretion (88 to 67 μg/L) at a low dose IL2. In a sub-analysis of the two age groups no effect on GH secretion in the older group was noted, in contrast to young subjects, especially on low dose IL2 (P=0.07). The analysis was refined further by calculating cumulative pulse masses in 2-h bins. By this approach it could be demonstrated that the cumulative GH pulse mass in older subjects across the 24 h was unchanged, while that in young subjects was temporarily inhibited in the bins between midnight and 0400 h (P=0.019 and 0.038). **Conclusion:** This study demonstrated that IL2 temporarily diminished GH secretion in young but not elderly volunteers. Pituitary hormone secretion by IL2 has not been studied as extensively as other cytokines, including IL1, IL6 and TNF. IL2 stimulates ACTH and TSH, inhibits LH and has no effect on GH secretion by rat pituitary (PNAS 58:185,1993). In patients with renal cancer IL2 infusion has no effect on GH levels (Anti-Cancer Res 10:753,1990. The present findings extend these observations to a large group of healthy volunteers, in whom we demonstrated previously suppression of the gonadal axis and activation of the HPA-axis (JCEM 101:539,2016, Endocr Connect 9:637,2010).

Neuroendocrinology and Pituitary

CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Improved Acromegaly Patient Satisfaction With Oral Octreotide Capsules Compared With Injectable Somatostatin Receptor Ligands in the MPOWERED Trial

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Background: Improved patient-reported outcomes (PROs) are increasingly becoming a key treatment objective in acromegaly. Validated PROs were used to assess disease and treatment burden in the MPOWERED phase 3 trial in acromegaly, which also assessed safety and efficacy of oral octreotide capsules (OOC; MYCAPSSA®) compared to injectable SRLs (iSRLs).
Methods: Eligible patients had acromegaly diagnosis, biochemical control of acromegaly (insulin-like growth factor I <1.3 × upper limit of normal; mean integrated growth hormone, <2.5 ng/mL) and ≥6 months' iSRL treatment (octreotide or lanreotide). Eligible patients entered a 26-week Run-in phase to determine the effective OOC dose; responders at week 24 then entered a 36-week randomized controlled treatment (RCT) phase receiving OOC or iSRLs in a 3:2 ratio. The Acromegaly Treatment Satisfaction Questionnaire (Acro-TSQ) is a recently validated tool that includes 27 items in 6 domain scores for PROs in acromegaly.[1] Acro-TSQ data were collected at baseline (reflecting outcomes on iSRLs), end of Run-in (reflecting outcomes on OOC), and end of RCT (OOC or iSRLs).
Results: Of 146 enrolled patients, 92 entered RCT (OOC, N=55; iSRLs, N=37). Acro-TSQ scores at the end of Run-in (26 weeks' OOC treatment) were compared to baseline (iSRLs). In the 92 patients randomized, 3 of 5 Acro-TSQ domains (emotional reaction, treatment convenience, and treatment satisfaction) showed significant improvement at end of Run-in compared to baseline. Injection site interference was not assessed as no injection site reactions were observed with OOC. Other domains showed a nonstatistically significant pattern of improvement at end of Run-in when compared to baseline. Patients randomized to iSRLs in the RCT after receiving OOC in the Run-in (N=37) reported more anxiety (RCT end, 53%; Run-in end, 29%) and frustration (RCT end, 45%; Run-in end, 34%) with iSRLs compared to OOC. Overall treatment satisfaction was higher while receiving OOC (Run-in end, 92%; after receiving iSRLs in RCT, 75%). Breakthrough symptoms were reported more frequently with iSRLs (31%) than OOC (15%) at the end of RCT.
Conclusion: Higher patient satisfaction, convenience and emotional well-being, and improved symptom control based on the newly validated Acro-TSQ PRO reporting tool were observed with OOC compared to iSRLs in patients enrolled in the MPOWERED trial.
[1]Fleseriu M, et al. *Pituitary*. 2020 Aug;23(4):347-358.

Neuroendocrinology and Pituitary

CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Long-Term Control of Urinary Free Cortisol With Osilodrostat in Patients With Cushing's Disease: Final Results From the LINC 2 Study

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Introduction: During the 22-week core LINC 2 study, the oral 11β-hydroxylase inhibitor osilodrostat normalized mean urinary free cortisol (mUFC) in 79% (15/19) of patients with Cushing's disease. This report describes long-term LINC 2 efficacy and safety results following an optional extension. **Methods:** Patients receiving clinical benefit at week 22 could enter the extension (that ran until Oct 22, 2019), continuing the same osilodrostat dose; dose adjustments were permitted based on efficacy and safety. Response rate (mUFC ≤ULN [controlled] *or* mUFC >ULN but ≥50% decrease from baseline [BL; partially controlled]) was assessed over time. Efficacy/safety were assessed for all patients from core BL until study end. **Results:** Of 19 enrolled patients (female:male 14:5; mean [SD] age 36.8 years [8.4]), 16 entered the optional extension and 8 of them remained on treatment until study end. Median (range) osilodrostat exposure was 282 weeks (2-351). Mean mUFC decreased from BL (9.9 x ULN) to ≤ULN by week 4 and remained stable throughout the study. All 19 patients achieved mUFC ≤ULN at least once during the study. At each assessment up to month 70 of the extension phase, 50-88% of ongoing patients were controlled, and up to 18% were partially controlled. Mean percentage change in clinical signs from BL (mean [SD]) to last assessment were: fasting plasma glucose, -10.8% (22.1) (from BL: 105.6 mg/dL [49.2]); HbA_{1c}, -2.1% (9.0) (from BL: 5.7% [0.7]); systolic BP, -3.3% (12.6) (from BL: 132.6 mmHg [11.6]); diastolic BP, -2.0% (10.4) (from BL: 85.0 mmHg [6.5]); BMI, -5.9% (8.8) (from BL: 30.7 kg/m^2 [7.0]). Overall, 9 patients discontinued treatment (n=2 core and n=7 extension), mostly because of AEs or no longer requiring treatment (n=3 each). The most common AEs during the entire treatment period were nausea (n=10), adrenal insufficiency, and headache (both n=9). AEs related to hypocortisolism and adrenal hormone precursor accumulation occurred in 11 (mostly adrenal insufficiency, n=9) and 12 patients (mostly hypertension, n=4), respectively; most were grade 1/2 and managed with dose adjustment/interruption and/or concomitant medication. Mean (SD) plasma ACTH increased from 1.8 x ULN (0.9) at BL to 7.1 x ULN (12.3) at week 22 and 6.9 x ULN (12.6) at last assessment. Mean (SD) 11-deoxycortisol increased from 1.2 x ULN (1.3) at BL to 13.6 x ULN (12.2) at week 22 and 3.6 x ULN (4.2) at last assessment. In females, mean (SD) testosterone increased from 0.8 x ULN (0.4) at BL to 2.4 x ULN (2.1) at week 22 and 1.0 x ULN (0.9) at last assessment. Two patients, both female, reported an AE of hirsutism.