patients (10 females, 12 males) completed a 1-year treatment. Mean age was 41.8±13.8 years. Twelve patients (54.5%) were ≤ 40 years old (including 6 (27.3%) patients of age ≤30 years). At baseline, mean IGF-1 level was 2.3 (SD 0.7) x ULN (age- and sex-specific) (583.9 ng/mL; SD 182.2) and mean GH concentration was 3.9 (SD 2.8) ng/mL. Both values decreased significantly after 1 year of treatment (P<0.001). Pasireotide LAR dose was increased to 60 mg in 16 (72.7%) patients and decreased to 20 mg in one patient patient due to worsening of diabetes control. The magnitude of mean GH level decrease was the largest within first 6 months (mean change from baseline: -1.75 ng/mL, 95% CI: -2.64, -0.85, P=0.0006). Mean IGF-1 level decreased rapidly within the first 3 months (mean change from baseline: -153.20 ng/mL, 95% CI: -203.20, -103.19, P<0.0001) and remained low during 12-month follow-up. GH level ≤ 1 ng/mL and ≤2.5 ng/mL was achieved by 7 (31.8%) and 17 (77.3%) patients, respectively. Six patients (27.3%) achieved normal IGF-1 level (IGF-1 ≤1 x ULN) (P=0.0275). IGF-1 ≤1.3 x ULN was observed in 11 (50.0%) of patients. Full biochemical control (GH ≤1 ng/mL and IGF-1 ≤1 x ULN) was achieved in 3 (13.6%) patients. Pasireotide LAR treatment resulted in significant increase of mean fasting glucose level: 119.2 (SD 17.3) vs. 107.5 (SD 13.9) mg/dL, P<0.001. The largest change was observed in first 3 months, and it remained stable until month 12. HbA1c level also increased significantly during first 3 months and stayed on similar level during follow-up (mean for month 12: 6.3 (SD 0.6) vs. 5.9 (SD 0.5) % at baseline, P<0.001). **Conclusions:** Pasireotide LAR is an effective treatment in most patients with persistent acromegaly after surgical debulking resistant to first generation SSAs. The largest increase of glycemia occurs during first 3 months of treatment and it remains stable afterwards.

Neuroendocrinology and Pituitary
CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Safety and Efficacy of Levoketoconazole in the Treatment of Endogenous Cushing's Syndrome (LOGICS): Results From a Double-Blind, Placebo-Controlled, Randomized Withdrawal Study

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Endogenous Cushing's syndrome (CS) is a rare, serious disorder caused by chronic cortisol excess. A phase 3, open-label study (SONICS) demonstrated efficacy and safety of levoketoconazole in adults with CS. LOGICS is a phase 3, double-blind (DB), placebo-controlled, randomized-withdrawal (R-W) study that investigated levoketoconazole in adults with CS via an open-label titration-maintenance (T-M) phase (14-19 weeks) followed by a DB R-W phase (~8 weeks) and a restoration phase (~8 weeks). The primary endpoint is the proportion of patients with loss of mean urinary free cortisol (mUFC) response during R-W (ie, mUFC ≥1.5x ULN or mUFC >40% above baseline if baseline was >1.0x ULN, or other rescue criterion met). Key secondary endpoints include mUFC normalization and changes in comorbidity biomarkers at the end of R-W. Of 84 patients dosed in LOGICS (12 SONICS-completers and 72 de novo), 79 were titrated (72 de novo) and 44 patients (39 from T-M and 5 direct roll-overs from SONICS) were randomized 1:1 to receive levoketoconazole (n=22) at an individualized therapeutic dose or a matching placebo regimen (n=22). The R-W population mean age was 44.3 years, 77% were female, 91% were white, mean weight was 83.2 kg, and 86% had Cushing's disease. Selected results from an interim analysis at the end of R-W are presented. At the end of R-W, significantly more patients on placebo (95.5%) achieved primary endpoint of loss of mUFC response than those who continued on levoketoconazole (40.9%) (treatment difference [TD], -54.5%; 95% CI: -75.7, -27.4; *P*=0.0002). Similarly, the mUFC normalization rate at the end of R-W was significantly higher for levoketoconazole (50.0%) versus placebo (4.5%; TD, 45.5%; 95% CI: 19.2, 67.9; *P*=0.0015). Mean change from R-W baseline to end of R-W in total cholesterol was -1.4 mg/dL for levoketoconazole and +35.6 mg/dL for placebo (*P*=0.0004); mean change in LDL cholesterol was -0.2 mg/dL and +25.0 mg/dL, respectively (*P*=0.0056). Mean change in glycemia markers and high sensitivity C-reactive protein were not significantly different between treatment groups. 90% of levoketoconazole-treated patients across the T-M and R-W phases (n=80) had ≥1 treatment-emergent adverse event (AE); AEs led to treatment discontinuation in 19% (15/80) of patients, 11% (9/80) of which were considered treatment-related. The most common AEs were nausea (29%), hypokalemia (28%), and headache (21%); serious AEs drug related were reported in 4 patients (3 liver-related, 1 gastroenteritis, 1 hypokalemia); AEs of special interest included liver-related (11%), QT prolongation (10%), and adrenal insufficiency (10%). These LOGICS interim results confirm the safety and efficacy findings from SONICS, establishing treatment benefit as levoketoconazole specific. This evidence further supports the use of levoketoconazole as an important treatment option for endogenous CS. **Support:** Strongbridge Biopharma.

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Safety and Efficacy of Switching Injected Peptide Long-Acting Somatostatin Receptor Ligands to Once Daily Oral Paltusotine: ACROBAT Edge Phase 2 Study