data, data on medications and regimens used to treat pituitary diseases, information on co-morbidities and concomitant medications used in 355 patients with various pituitary diseases: prolactinomas, clinically nonfunctional adenomas (CNFA), acromegalies, empty sella syndrome, Cushing's disease (CD), Ratke's pocket cysts, meningiomas, craniopharyngoma, pituitary aplasia and hypoplasia, TSH-omas, germinoma, glioma, chondrosarcoma, pericytoma. **Results:** From July 2016 to July 2019, 355 people (71.7% women) with pituitary diseases were registered. The mean age in the cohort was 43.4 yrs (range 18–83 yrs). Prolactinomas were the most common adenomas (40.8%), followed by CNFA (28.5%), acromegaly (16.1%) and empty sella syndrome (5.1%), CD (2.3%), Ratchet pocket cysts (2.3%), meningiomas (1.4%), craniopharyngiomas (1.1%), pituitary aplasia and hypoplasia (0.8%), TSH-omas (0.6%), germinoma (0.3%), glioma (0.3%), chondrosarcoma (0.3%), pericitoma (0.3%). Female dominance was observed in patients with prolactinoma and CNFA, empty sella syndrome, Ratke's pocket cysts, CD, meningiomas, TSH-omas. Patients in the cohort most often received drug therapy with any type of medication alone (octreotide LAR, lanreotide, bromocriptine, cabergoline, pegvisomant) in 50.5% of cases; various types of combination therapy in 13% of cases. The majority of patients (81.7%) were treated with 1or more medication for co-morbidity. Thyroid disease was slightly more common than cardiovascular disease: 86.1% vs. 81.3%. In 10.1% of the cohort, cancer of various localities was detected. Both types of diabetes or other disorders of carbohydrate metabolism were found in 36.3% of cases. **Conclusion:** Based on the study of the pituitary disease register in Latvia, a unified database of pituitary disease patients has been created, which allows analyzing the population characteristics of the pituitary diseases, the applied treatment schemes for the treatment of pituitary diseases; types of neurosurgery, medication and radiation therapy. A state register may be set up in the future.

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Prevalence of the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) in Patients With Brucellosis: A Meta-Analysis

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Background: Hyponatremia is prevalent amongst hospitalized patients and is associated with adverse outcomes. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a common cause of hyponatremia. In our experience in a middle eastern country, we observed a relationship between brucellosis and SIADH associated hyponatremia. Nonetheless, there is limited literature describing this association. Thus, we aimed to systematically review the literature and pool the prevalence of SIADH in patients with brucellosis. **Methods:** We comprehensively searched PubMed, EMBASE, and Google scholar (first 100 hits) for observational studies ascertaining the prevalence of SIADH in brucellosis patients. We had no age, language, or date limitations. We used a proportion meta-analysis utilizing the random-effects model with double arcsine transformation. I^2 was used to ascertain heterogeneity. We used MetaXl software for statistical analysis. The protocol was preregistered at PROSPERO. **Results:** Our search in PubMed and EMBASE retrieved 107 articles, of which only four observational studies were relevant. Aysha et al. conducted the first analysis of 58 brucellosis patients in which 24% had sodium levels of less than 130 mmol/L. We excluded this study from our quantitative synthesis as the SIADH prevalence could not be accurately ascertained. Finally, the quantitative synthesis comprised three studies encompassing 306 patients and revealed a pooled SIADH prevalence of 20% (95% CI 0-52%, I^2 96%). The quality assessment revealed low to moderate quality of included studies. **Conclusion:** The reported prevalence of SIADH in individual studies included in our analysis ranged from 3-56%. The results were heterogeneous, as depicted by a high I^2. This varying prevalence is perhaps due to the varying age of included participants, definitions used by the primary studies, and the included data's observational nature. Nonetheless, our meta-analysis revealed a relatively high prevalence of SIADH of 20% in patients with brucellosis. Hence, hyponatremia in patients with chronic fever should prompt a workup for SIADH and brucellosis, especially in endemic areas for brucellosis. Larger prospective studies are needed to ascertain the exact prevalence of SIADH in this patient cohort and its impact on the overall prognosis.

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Real-World Experience With Pasireotide Lar in Acromegaly Resistant to First-Generation Somatostatin Analogs: A Single Center 1-Year Observation

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Introduction: First generation somatostatin analogs (SSAs) are the treatment of choice in persistent acromegaly after transsphenoidal surgery. However, they are effective in 25% to 45 % of patients and a second generation SSA - pasireotide LAR may be a more effective alternative. Aim Our aim was to evaluate the impact of 1-year treatment with pasireotide LAR on disease control and on glucose metabolism in patients with acromegaly after debulking surgery resistant to first-generation SSAs. Material and methods In this single-center prospective study 29 consecutive patients with resistant acromegaly were treated with pasireotide LAR. The initial drug dose was 40 mg i.m. every 28 days. If patient did not achieve biochemical control (GH <2.5 ng/mL and IGF-1 ≤ULN for age and sex) at month 3, the dose was increased to 60 mg i.m. every 28 days. Assessment (GH, IGF-1, glucose, HbA1c) was performed at month 3, 6, 9 and 12. **Results:** In total, 22

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.

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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