insufficient numbers of subjects to examine the effect of race on the teprotumumab proptosis response. All analyses were performed on the intent-to-treat (ITT) population using data from the study eye.

Results: A total of 171 patients comprised the population from the two studies. Eighty-four and 87 patients were randomized to the teprotumumab and placebo groups, respectively, and the treatment groups had balanced baseline characteristics. At week 24, significantly more teprotumumab than placebo patients were proptosis responders in all examined subgroups (male: 73.1% vs. 5.0%, female: 79.3% vs. 17.9%, smokers: 70.0% vs. 23.1%, non-smokers 79.7% vs. 11.5%, younger: 76.1% vs. 16.2%, older: 84.6% vs. 7.7%; all $p < 0.001$). In continuous variable analyses, the mean proptosis reduction from baseline was also significantly greater at week 24 in teprotumumab-treated patients than placebo patients (male: -3.34 vs. -0.07 mm, female: -3.10 vs. -0.42 mm, smokers: -2.99 vs. -0.72 mm, non-smokers: -3.20 vs. -0.31 mm, younger: -3.10 vs. -0.39 mm, older: -3.55 vs. -0.22 mm; all $p < 0.001$).

Conclusion: Teprotumumab was effective across subgroups of age, gender, and smoking status in the pooled 24-week clinical trials.

Reference: (1) Smith TJ, et al. *N Engl J Med* 2017;376:1748-1761. (2) Douglas RS, et al. AACE 2019 late-breaking abstract. (3) Kahaly GJ, et al. *Thyroid* 2019;29(Suppl1):A-1 [abstract].

Cardiovascular Endocrinology

FROM BEDSIDE TO BENCH AND BACK AGAIN: LIPID METABOLISM & VASCULAR DISEASE

Changes in Hepatokines and Apolipoproteins Are Associated with Metabolic Response to Metreleptin in Partial Lipodystrophy

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OR17-02

Introduction Metreleptin treatment may improve the metabolic aspects of partial lipodystrophy; however, the treatment response is heterogeneous. This study aimed to explore changes in circulating apolipoprotein concentrations, as well as ANGPLT3, ANGPLT4, and IGF-1 levels in patients treated with Metreleptin as part of a clinical study investigating the efficacy of Metreleptin in non-alcoholic steatohepatitis (NASH) associated with partial lipodystrophy (ClinicalTrials.gov identifier: NCT01679197).

Methods Serum samples of 18 patients with partial lipodystrophy who underwent a full metabolic evaluation and paired liver biopsies before and after Metreleptin were studied. Patients were tested at baseline, month (M) 3, M6, and M12. Glycemic response was defined as "more than 1% HbA1c reduction from baseline". Lipid response was defined as "more than 30% decrease in triglycerides from baseline". The hepatic response was defined as "a decrease of 2 points or more from baseline in NASH score, without an increase in fibrosis". Patients with "any 2 of 3 above" at M12 were defined as metabolic responders. **Results** Metreleptin treatment resulted in significant reductions in triglycerides (346 mg/dL vs. 253 mg/dL; F: 8.474; $p < 0.001$), apo B (145.24 mg/dL vs. 111.09 mg/dL; F: 9.266: $p < 0.001$), apo CII (18.65 mg/dL vs. 15.95 mg/dL; F: 6.663: $p = 0.001$), apo CIII (62.95 mg/dL vs. 49.33 mg/dL; F: 5.640, $p = 0.002$), apo E (8.16 mg/dL vs. 6.52 mg/dL; F: 11.056, $p < 0.001$), and ANGPLT3 (14.36 ng/mL vs. 12.00 mg/dL; F: 4.348; $p = 0.008$) over time. IGF-1 levels significantly increased at M3 (134 ng/mL vs. 139 ng/mL; $p = 0.001$), however the difference was not significant over time. Metabolic responders had lower baseline leptin (12.4 ng/mL vs. 27.8 ng/mL; $p = 0.024$) and IGF-1 (95 ng/ml vs. 151 ng/mL; $p = 0.008$), and higher apo CII (39.06 mg/dL vs. 17.90 mg/dL; $p = 0.011$), apo CIII (173.57 mg/dL vs. 51.51 mg/dL; $p = 0.015$), apo E (18.41 mg/dL vs. 5.89 mg/dL; $p = 0.002$), and ANGPLT3 (17.33 ng/mL vs. 10.06 ng/mL; $p = 0.04$). Metabolic responders had a significant increase in IGF-1 (95 ng/mL vs. 134 ng/mL; $p = 0.019$), which was statistically distinguished from non-responders ($p = 0.004$). Responders also had a greater reduction in apo CII (20.51 mg/dL vs. -1.84 mg/dL; $p = 0.001$), apo CIII (32.59 mg/dL vs. -7.83 mg/dL; $p = 0.007$), apo E (8.17 mg/dL vs. 0.22 mg/dL; $p = 0.001$), and ANGPLT3 (6.08 ng/mL vs. -0.16 ng/mL; $p = 0.005$) early after treatment at M3. **Conclusions** Metreleptin treatment lowers levels of apolipoproteins associated with triglyceride metabolism as well as ANGPLT3 in patients with partial lipodystrophy. Metabolic response to Metreleptin appears to be correlated with early changes in these factors and an increase in IGF-1 levels.

Adrenal

ADRENAL CASE REPORTS II

Intra-Articular Triamcinolone Injections - a "Slipped" Cause of Cushing's Syndrome

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SUN-188

Background:
Triamcinolone injections are used to treat various orthopedic and rheumatologic conditions; their effects on the hypothalamic pituitary adrenal axis have not been well characterized.
Clinical Case:
A 14 yo female was referred to our clinic for evaluation of low TSH (0.16 μIU/mL) and possible hyperthyroidism. There was no goiter and she appeared euthyroid and had normal free T4 (1.01 ng/dl) but she had typical features of Cushing syndrome (CS), including round facies, thinning of hair, fatigue, truncal adiposity, violaceous striae, facial hirsutism and oligomenorrhea. She was previously healthy and participated in many sports. She did not report any history of exogenous glucocorticoid use but the fasting ACTH (4 pg/ml) and cortisol (0.1 μg/dl) levels were suppressed. Subsequent chart review revealed that she received intra-articular Triamcinolone (TA) to treat "slipping rib" syndrome. This included 3 injections of Kenalog 40 mg/mL, the last in July 2019. Her cumulative TA dose was 440 mg, the equivalent of prednisone 550 mg. Triamcinolone acetonide 1.4 mcg/dL (normal 0-0.1, analyzed by LC-MS/MS) was detected in the urine over 3 months after her last injection.

Conclusion:
- Levels of ACTH and cortisol can be suppressed for several months after intra-articular corticosteroid injections, placing the patient at subsequent risk for adrenal crisis
- In some cases, high doses of Triamcinolone administered by intra-articular injection can cause clinical Cushing syndrome

Diabetes Mellitus and Glucose Metabolism

LIPIDS, OBESITY AND METABOLIC DISEASE

Bile Acid Sequestration Synergistically Accelerates Glucagon Receptor-Stimulated Body Weight Loss in Diet-Induced Obese Mice

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SAT-655

Glucagon, an essential regulator of glucose and lipid metabolism, also promotes weight loss in obese mice. We have shown that hepatic Farnesoid X Receptor (FXR, a bile acid receptor) and bile acids (BA) play an important role in the anti-obesity effect of glucagon in mice. Specifically, glucagon-receptor (GCGR) agonism is a potent regulator of BA metabolism, increasing total plasma BA levels and preferentially raising cholic and chenodeoxycholic acid levels. These findings led us to hypothesize that BA, signaling via hepatic FXR, contributes to GCGR-stimulated weight loss. Furthermore, we reasoned that BA sequestration may impair GCGR-mediated weight loss by reducing the availability of BA to stimulate FXR-action. Thus, to elucidate the role of BA in GCGR-mediated weight loss, we utilized anion-exchange BA-binding resins (BARS; Cholestyramine and Colesevelam) to prevent intestinal (ileal) re-uptake and reduce plasma total cholesterol, LDL, and BAs via fecal excretion. Diet-induced obese (DIO) C57Bl/6J mice were randomized to groups matched for body-weight and administered daily GCGR agonism (IUB288, 10 nmol/kg, s.c.) or vehicle, in the presence or absence of BARS. Consistent with our prior findings, IUB288-treatment reduced body weight in DIO mice. Counter to our original hypothesis, IUB288+Cholestyramine (3% in high fat diet, HFD [58% kcal%]) enhanced IUB288-stimulated weight loss. Similar body-weight loss effects following combined IUB288 and BARS treatment were replicated both at a lower dose of Cholestyramine (1.5% in HFD), as well as in combination with both low- (2% in HFD) and high- (4% in HFD) dose Colesevelam. IUB288-stimulated weight loss is accompanied by suppression of food intake (FI), while Colesevelam alone did not significantly lower FI at either dose (2 or 4% in HFD). However, 4% Colesevelam with IUB288 completely suppressed FI, while 2% Colesevelam stimulated a reduced, though not complete suppression. GCGR agonism is a potent stimulus of weight loss; however, its impairment of glucose tolerance reduces its value as a monotherapy. Excitingly, Cholestyramine (3% in HFD) rescued IUB288-induced glucose intolerance, restoring glucose excursion to levels observed in control (vehicle-treated) mice. Together these studies suggest BARS may enhance the anti-obesity effect of GCGR agonism, beneficially regulate feeding behaviors, and prevent GCGR-stimulated glucose dysregulation in DIO mice. Furthermore, these studies argue that GCGR agonsim combined with BARS treatment may represent a novel therapeutic approach for obesity and obesity-associated glucose intolerance.

Neuroendocrinology and Pituitary

CASE REPORTS IN CLASSICAL AND UNUSUAL CAUSES OF HYPOPITUITARISM

Combination of Immune Check Point Inhibitors Causing Hypopituitarism

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SAT-239

Introduction: Immune Check Point inhibitors (ICI) have been associated with immune related adverse events including a wide array of Endocrinopathies particularly when a combination of ICIs is used. We present a case of Hypopituitarism secondary to CTLA-4 inhibitor Iplimumab and PD-1 inhibitor Pembrulizumab in a patient with Vulvar Melanoma.

Case Description: 49-year-old female with past medical history of Type 2 Diabetes and Vulvar Melanoma presented with nausea, vomiting and fatigue. The patient had surgical excision of Vulvular Melanoma and had been on chemotherapy with Pembrolizumab and Ipilimumab for 1 month. She was found to be hypotensive in the ER, but blood pressure improved after fluid resuscitation. Her blood sugar levels were 76 MG/DL. She denied using any insulin in the last 24 hours. AM Cortisol was <1 UG/ML. TSH was 0.205 UIU/ML with free T4 at 0.74 NG/DL. FSH was 2.5 MIU/ML. LH was 0.5 MIU/ML. Prolactin was 90.2 NG/ML. ACTH was less than 9 PG/ML. MRI of the brain showed mildly enlarged pituitary gland with suprasellar extension, measuring 10.5 mm in craniocaudal height and normal homogeneous enhancement. A diagnosis of Hypopituitarism secondary Ipilimumab and Pembrolizumab was made. She was started on steroids and thyroid replacement. The patient's symptoms resolved, and she was discharged home in a stable condition with outpatient Endocrinology follow up.

Discussion: Immune checkpoint inhibitors (ICI) includes PD1(Programmed cell death receptor 1) inhibitors like Pembrolizumab and CTLA-4 (Cytotoxic T Lymphocyte Antigen-4) inhibitors like Ipilimumab. CTLA-4 inhibitors have more frequently been associated with Hypophysitis leading to particularly ACTH and TSH deficiencies and causing secondary adrenal insufficiency and secondary hypothyroidism. Posterior Pituitary involvement is less common. MRI usually shows mild to moderate enlargement of the pituitary gland. ICI therapy usually does not need to be stopped. Patients commonly require long term glucocorticoid and thyroid replacement.