overexpression of the one located closely to the olfactory receptor 1322 gene exerted in a mouse hepatoma cell line the robust transcriptional regulatory activity on ~100 protein-coding genes that were accumulated in several distinct biological pathways. Our results indicate that mouse serum contains biologically active intergenic sncRNAs in addition to other known forms. The results also suggest their potential biological importance and/or usefulness in disease diagnosis and treatment in humans.

Diabetes Mellitus and Glucose Metabolism

TYPE 1 DIABETES MELLITUS

Anti PD1 Induced Type 1 Diabetes

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SAT-674

Introduction: Pembrolizumab t is used to treat various cancers. It is associated with immune related adverse events (IRAEs) that can be life threatening [1,4]. We describe a patient who presented autoimmune Diabetes after the use of Pembrolizumab. **Case:** 64 y/o African American female PMHX of lung non-small cell lung cancer diagnosed in 2017 Clinical stage IV with gluteal metastasis, and dementia. Pt was referred by Oncology. The patient had a family history of Type 1 DM. and complained of dizziness, and unintentional weight loss (30 pounds) over a year. She had received 2 cycles of Pembrolizumab. The last cycle given 5 weeks before presentation to Endocrinology. Physical examination revealed cachectic female (weight 35 kg, height 147cm), dry mouth, BP 135/82, Plasma glucose 383mg%, A1c 7, negative Islet cell antibodies, positive anti-GAD, undetectableserum C-peptide. Cortisol 27, Acth 21 at 8 am and TSH 2.3. **Discussion:** In a systematic literature review, the early pattern of Diabetes onset with the use of checkpoint inhibitors was evaluated and on average after 4.5 treatment cycles [4].The incidence of immune checkpoint inhibitor-induced Type 1 Diabetes is estimated at 1% [3].This appeared to be earlier for the combination of anti-cytotoxic T-Lymphocyte associated antigen 4 monoclonal antibody and PD-1 therapy. The onset of β cell inflammation is often fulminant, suggested by the relatively low glycated hemoglobin levels, while C-peptide levels are usually low or undetectable at diagnosis and mostly positive GAD antibodies [5]. This side effect is predominantly found in patients exposed to blockade of the PD-1/PD-Ligand pathway. The IRAEs are primarily managed by immunosuppression with corticosteroids and discontinuation of immunotherapy except in autoimmune Diabetes which is irreversible. Physicians should be aware of and patients educated about the important multiorgan side effects since a growing number of patients are treated with checkpoint blockade.Azoury SC, Straughan DM, Shukla V. Immune checkpoint inhibitors for cancer therapy: clinical efficacy and safety. *Curr Cancer Drug Targets* 2015;15: 452-462Weber JS, Postow M, Lao CD, et al. Management of adverse events following treatment with anti-programmed death-1 agents. *Oncologist* 2016;21:1230-40Stamatouli AM, Quandt Z, Perdigoto AL, Clark PL, Kluger H,Weiss SA et al Collateral damage: insulin-dependent diabetes induced with checkpoint inhibitors. *Diabetes* 2018;67(8):1471-1480de Filette JMK, Pen JJ, Decoster L, et al. Immune checkpoint inhibitors and Type 1 Diabetes mellitus: a case report and systematic review. *Eur J Endocrinol.* 2019;181(3):363–374. Akturk HK, Kahramangil D, Sarwal A, Hoffecker L, Murad MH, Michels AW. Immune checkpoint inhibitor-induced Type 1 Diabetes: a systematic review and meta-analysis. *Diabet Med.* 2019;36(9):1075–1081.

Adipose Tissue, Appetite, and Obesity

MECHANISMS AND TREATMENT OF OBESITY IN HUMANS

Liraglutide for Weight Management in Pubertal Adolescents with Obesity: A Randomized Controlled Trial

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OR33-01

Background: Pediatric obesity is a chronic disease with rising prevalence and limited treatment options; first-line intervention is lifestyle therapy, which is typically unsuccessful.[1] Liraglutide (3.0 mg) as an adjunct to lifestyle therapy has provided weight loss and improved cardiometabolic risk factors in adults.[2] Here we report the results of liraglutide 3.0 mg in adolescents with obesity who failed to respond to lifestyle therapy.

Methods: A multinational, randomized, double-blind trial (NCT02918279) with a 12-wk run-in of lifestyle therapy, 4-8-wk dose escalation, 52-wk maintenance period and 26-wk follow-up off trial drug. Adolescents aged 12-<18 years with obesity, stable weight and suboptimal response to lifestyle therapy alone were randomized 1:1 to once-daily subcutaneous liraglutide 3.0 mg (or maximum tolerated dose) or placebo (PBO), both as an adjunct to lifestyle therapy. Randomization was stratified by pubertal and glycemic (normal vs prediabetes/type 2 diabetes) status. Primary endpoint was change in BMI standard deviation score (SDS)[3] from wk 0 to 56.

Results: Of 125 adolescents randomized to liraglutide 3.0 mg and 126 to PBO, 101 and 100 completed treatment at wk 56, respectively; 99 in each arm completed the trial at wk 82. 40.6% were male; mean age 14.5 years; mean BMI 35.6 kg/m^2; mean BMI SDS 3.17. Liraglutide 3.0 mg was superior to PBO for change in BMI SDS at wk 56 (estimated treatment difference [ETD] -0.22; 95% CI -0.37, -0.08; p=0.0022). In the liraglutide 3.0 mg vs PBO arm, 43.25% vs 18.73% (p=0.0002) and 26.08% vs 8.11% (p=0.0006) of adolescents had ≥5% and ≥10% reduction in

baseline BMI at wk 56, respectively. A significant difference in change in BMI was seen for liraglutide 3.0 mg vs PBO: ETD -4.64%; 95% CI -7.14, -2.14; p=0.0003. A significant reduction in waist circumference with liraglutide 3.0 mg was shown at wk 56 (p=0.0126). Greater weight regain/rebound in BMI SDS at wk 82 was seen for liraglutide 3.0 mg vs PBO after drug discontinuation (ETD 0.15; 95% CI 0.07, 0.23; p=0.0002). There were no significant differences in blood pressure, fasting lipids, fasting plasma glucose or HbA1c at wk 56. No unexpected safety concerns and no severe hypoglycemia were reported. During treatment (0–56 wks), more adolescents in the liraglutide 3.0 mg (64.8%) vs PBO arm (36.5%) reported gastrointestinal adverse events (AEs), and 3 vs 5 adolescents, respectively, reported serious AEs. Mental health questionnaire results were similar in both arms at wk 56. No effect on growth or pubertal development was found.

Conclusions: This trial demonstrates clinically meaningful[4] weight loss in adolescents with obesity treated with liraglutide 3.0 mg as an adjunct to lifestyle therapy. The safety profile was similar to that observed in adults.

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Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

Association of Baseline Cardio-Metabolic Parameters on the Treatment Effects of Empagliflozin When Added to Metformin in Patients with T2D

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MON-645

Sodium-glucose co-transporter-2 inhibitors (SGLT2i) are commonly used as 2nd-line therapy after metformin (MET) in patients with type 2 diabetes (T2D), and are now recommended in those with co-existing cardiovascular (CV) and/or chronic kidney disease (CKD). A better understanding of their clinical efficacy across the spectrum of cardio-metabolic characteristics may help to better individualize therapy. It was previously reported (Häring *et al., Diabetes Care* 2014) that empagliflozin (EMPA) 10 and 25 mg over 24 weeks vs placebo (PLB), when added to MET, led to clinically meaningful improvements in HbA1c, body weight (BW), and systolic blood pressure (SBP).

We explored the magnitude of these effects across categories of baseline (BL) HbA1c, BW, and SBP, comparing EMPA 10 mg (n=217) and 25 mg (n=213) vs PLB (n=207) in the following subgroups: HbA1c <8.5% and ≥8.5%; BW ≤70, 70-≤80, 80-≤90, and >90 kg; and SBP <120, 120-<140, and ≥140 mmHg. Analyses were performed for all randomized patients receiving ≥1 dose of study drug. Differences between treatment groups were assessed using ANCOVA and interaction tests (by respective BL factor and treatment-assignment). At week 24, EMPA 10 mg and 25 mg significantly (p<0.0001) reduced HbA1c vs PLB; the difference from PLB in adjusted mean [±SE] change was greater in the ≥8.5% vs <8.5% subgroup (EMPA 10 mg: -0.73 [±0.14]% vs -0.51 [±0.08]%, respectively; EMPA 25 mg: -0.97 [0.15]% vs -0.52 [0.08]%, respectively; interaction p: 0.029). EMPA also significantly (p<0.05) decreased BW vs PLB, with a trend for larger reductions in those with the highest BW at BL (EMPA 10/25 mg: -1.31 [±0.42]/-1.70 [±0.44], -1.23 [±0.53]/-0.74 [±0.54], -2.12 [±0.60]/-2.56 [±0.56] and -2.11 [±0.46]/-2.93 [±0.47] for ≤70, 70-≤80, 80-≤90, and >90 kg, respectively; interaction p: 0.075). Finally, EMPA significantly (p<0.05) lowered SBP vs PLB, but, in contrast, without significant differences across SBP categories (EMPA 10/25 mg: SBP <120 mg, -4.17 [±2.07]/-2.71 [±2.15]; SBP 120-<140, -4.35 [±1.48]/-4.98 [±1.49]; SBP ≥140, -4.28 [±2.38]/-6.29 [±2.33] mmHg; interaction p: 0.784). The number of patients reporting ≥1 adverse event (AE) was similar across treatment groups (PLB, 58.7%; EMPA 10 mg, 57.1%; EMPA 25 mg, 49.5%) and the AE profile was consistent with the drug's established safety profile. Confirmed hypoglycemic AEs were reported in 0.5%, 1.8%, and 1.4% of patients, respectively.

These data suggest that EMPA, when used as 2nd-line therapy after MET, is more effective in decreasing HbA1c and reducing BW in those with higher baseline values of these parameters but not for SBP. In addition to EMPA being a glucose-lowering agent recommended in patients with co-existing CVD and/or CKD, these data may help to tailor therapy as regards to important metabolic efficacy considerations.

Pediatric Endocrinology

UNDERSTANDING AND TREATING PEDIATRIC GROWTH DISORDERS

Mild Maternal Sleep Disordered Breathing in Pregnant Women Affects Growth Patterns of Head Circumference and Adiposity During the First Three Years of Life

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OR10-01

Background

The intrauterine environment affects growth and adiposity acquisition from the fetal period until adulthood. Mild sleep disordered breathing (SDB) during pregnancy is a common underdiagnosed medical condition in healthy women. We aimed to investigate the interaction between maternal isolated SDB during the third trimester of pregnancy and the offspring's growth and adiposity during the first three years of life.