was higher in patients with primary polydipsia versus controls and lower on dulaglutide versus placebo, but functional neuronal activity was similar between groups and treatments. **Conclusion:** GLP-1 receptor agonists reduce fluid intake and thirst perception in patients with primary polydipsia and could therefore be a novel treatment option for these patients.

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Metyrapone Treatment in Endogenous Cushing's Syndrome: Results at Week 12 From PROMPT, a Prospective International Multicenter, Open-Label, Phase III/IV Study

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Background: Metyrapone is a steroidogenesis inhibitor approved in Europe for the treatment of endogenous Cushing's syndrome (CS) based on observational retrospective studies published over more than 50 years. We present data from the first prospective study designed to confirm metyrapone efficacy and good tolerance in patients with CS.
Methods: This single arm, open-label, multicenter, international trial enrolled 50 patients with CS who had three baseline 24 hours urine free cortisol (UFC) values at least 50% above the upper limit of normal (ULN=165 nmol/24h). Metyrapone was titrated over 12 weeks (W12) to achieve normal urine (mean of 3 values, mUFC) and serum cortisol levels. Patients whose mUFC did not exceed 2-fold the ULN could enter a 6-month extension period. The primary efficacy endpoint was the proportion of patients with mUFC ≤ ULN at W12 assessed in a central laboratory using LC-MS/MS. The most important secondary endpoint was mUFC decrease of ≥ 50% at W12.
Results: At baseline: mean age was 47 years, median mUFC (range) was 570 (291 - 8476) nmol/24h (3.5 x ULN). Hypercortisolism was in 96% of patients either moderate (mUFC ≥ 2xULN; < 5x ULN) in 63% or severe (≥5 x ULN) in 33%. Hypertension (69%) and diabetes mellitus (47%) were the most common comorbidities. At W12: 47% (23/ 49) met primary endpoint. Another 40% (19 / 49) had mUFC ≤ 2xULN. Median percentage decrease in mUFC from baseline to W12 was -74%. Secondary endpoint was met by 80% of patients who had a mUFC decrease of 50%. Final median metyrapone dose was 1500 (250; 5500) mg/day. Physical signs and symptoms were normalized or improved in 66% of patients. Circulating cholesterol, HbA1C and fasting glucose and insulin improved with median decrease of 12%, 3%, 5% and 9% respectively and median systolic and diastolic blood pressure also decreased by 4 and 5mmHg respectively. Among patients with antihypertensive treatments, 10 (31%) had a decrease in number of drugs and 5 (16%) had an increase in number of drugs during the study. Median ACTH increased by 11 % from baseline.
Twenty six (52%) patients experienced mild to moderate study drug related adverse events (AEs). One patient discontinued before W12 because of an unrelated SAE on day 2 (pneumonia with septic shock). The most common AEs were nausea (24%), decreased appetite (18%), fatigue (14%), headache (10%), peripheral edema (6.0%), hypokalemia (6.0%) and hypertension (6.0%). Reversible adrenal insufficiency occurred in 6 (12%) patients. Few patients 14% (7/50) experienced at least one AE that led to a dose interruption or dose adjustment. Cushing Quality of Life Questionnaire increased of 10 points from baseline which is close to minimal clinically important difference = 10.1. **Conclusions:** This prospective study in patients with CS confirms that metyrapone effectively lowers UFC levels with a tolerability profile similar to the previously reported safety profile and improves QoL, at Week 12.

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