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IMPROVEMENTS IN HYPERTENSION AND DIABETES MELLITUS WITH OSILODROSTAT IN PATIENTS WITH CUSHING'S DISEASE: EXPLORATORY ANALYSES FROM THE PHASE III LINC 3 STUDY

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OBJECTIVES
This study aimed to explore blood pressure (BP) and glucose homeostasis changes with osilodrostat therapy in patients with Cushing's disease (CD) with baseline hypertension and diabetes mellitus (DM) during LINC 3 (nct02180217).

METHODOLOGY
Adult patients with CD with mean urinary free cortisol (MUFC) >1.5x ULN received osilodrostat for 48 weeks (w). Baseline hypertension was defined as a prior diagnosis of hypertension, use of antihypertensive medication, and/or SBP/DBP >130/>90 mm Hg. Baseline DM was defined as a prior diagnosis of T2DM, use of antidiabetic medication, HbA1C ≥6.5%, and/or FPG ≥126 mg/dl.

RESULTS
At baseline, 119/137 patients (87%) had hypertension. Mean SBP/DBP decreased with osilodrostat therapy. Baseline SBP >130 mm Hg (n=79) decreased to ≤130 mm Hg at w12, w24 and w48 in 58%, 51% and 49% of patients respectively. Baseline DBP >90 mm Hg (n = 50) decreased to ≤90 mm Hg at w12, w24 and w48 in 72%, 62% and 66% of patients respectively. Blood pressure did not increase in patients without baseline hypertension. An equal number (n = 34[40%]) stopped or reduced the dose of the medication and increased the dose/number of antihypertensives during the study among the 85 patients taking antihypertensives prior to recruitment. At baseline, 61/137 patients (45%) had DM. FPG decreased from ≥100 mg/dl at baseline (n = 36) to <100 mg/dl by w12, w24 and w48 in 58%, 64% and 44%, respectively. More patients taking antihyperglycemics at baseline stopped/reduced the dose (n = 21/43[49%]) compared to those who increased the dose/number of antihyperglycemics during the study (n = 10/43[23%]). Neither change in BP nor blood glucose parameters correlated with changes in UFC from baseline.

CONCLUSIONS
Consistent improvements in comorbid hypertension or DM occurred in many patients with CD receiving osilodrostat for 48 weeks. Concomitant adjustments in medications for hypertension and DM were required in some patients, including for those with improvements in the status of these comorbid conditions.