OP-3-5

ASSOCIATION BETWEEN GLUCOCORTICOID DOSE WITH BMI AND GLUCOCORTICOID-RELATED COMORBIDITIES: DATA FROM TILDACERFONT PHASE 2A TRIALS IN CLASSIC CONGENITAL ADRENAL HYPERPLASIA

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OBJECTIVES
Classic CAH treatment requires cortisol replacement to prevent life-threatening adrenal crises. However, the absence of cortisol feedback loop leads to persistent HPA activation and overproduction of adrenal androgens. Current treatment requires lifelong exposure to supraphysiologic glucocorticoid (GC) doses to suppress adrenal androgens.

Tildacerfont, an oral once-daily CRFR1 antagonist, decreased ACTH and androgens in patients with CAH in clinical trials, raising the possibility of improving disease control while decreasing the risks associated with lifelong GC exposure. This study describes GC-associated risks in the trial populations.

METHODOLOGY
This post-hoc, cross-sectional analysis characterizes the comorbidity profiles of subjects in two phase 2 studies stratified by GC dose.

RESULTS
Twenty-six adult participants, 58% female with an average age of 37 years [range 18-66], had a mean GC dose of 30.6 mg HCe/d [range 10-60 mg]. Evaluation by baseline GC dose [<30 mg (n = 9), ≥30 mg (n = 17)] showed trends toward higher BMI in the higher dose group, 32 vs. 29 kg/m^2, with more subjects meeting the criteria for obese II/III designation in the high dose group, 22% vs. 29%.

Trends were apparent in the baseline comorbidities reported in medical history: psychiatric disorders, including depression, anxiety, ADHD, and insomnia, occurred in 2/9 (22%) vs 8/17 (47%), obesity occurred in 3/9 (33%) vs. 8/17 (47%). Cushingoid features were reported in 0/9 vs 2/17 (12%). Both patients with Cushingoid features were on dexamethasone. Osteopenia/osteoporosis was reported in 1/9 (11%) vs 5/17 (29%). No meaningful differences were noted in baseline medications used.

CONCLUSIONS
In these studies, subjects with a higher GC dose exhibited a higher BMI and reported more GC-related comorbidities.