**INTRODUCTION**

- Olsodrostat (L696,122) is an oral inhibitor of 11β-hydroxysteroid dehydrogenase (the enzyme responsible for catalyzing the final step of cortisol catabolism).
- Olsodrostat also inhibits aldosterone synthesis by reversibly binding to aldosterone synthase.

- In a 22-week, Phase II study (LINC-2), olsodrostat normalized mean urinary free cortisol (mUFC) levels in 79% (16/19) of patients with Cushing’s disease.
- Here, we report safety and efficacy results of an interim analysis at month 18 in patients who entered an extension to LINC-2.

**METHODS**

**Study Design and Participants**

- Open-ended extension to LINC-2; a prospective, open-label, 22-week study in patients with Cushing’s disease.
- Patients could enter the extension if considered by the investigator to be receiving clinical benefit at week 22.
- Patients continued on the same dose of olsodrostat as at week 22.
- Dose adjustments were permitted during the extension (minimum: 1 mg once daily; maximum: 10 mg daily).

**Assessments and Statistical Analysis**

- Efficacy/safety are presented for patients who entered the extension.
- Response rate: sum of controlled (mUFC < upper limit of normal [ULN]) and partially controlled (mUFC > ULN and >50% reduction from baseline) patients.
- Response rate at month 19 was assessed with (LINC-2) and without (mUFC-ULN) imputation of missing values using last available measurements.
- Escape from response: mUFC-ULN on >2 consecutive visits on highest tolerated dose after previous mUFC normalization.
- AE: adverse events reported from baseline until last patient reached month 19.

**RESULTS**

**Patients**

- 16 of 17 patients (male/female: 5/11) who completed week 22 entered the extension.
- Median duration of olsodrostat treatment: 19.7 months (range: 0.8–25.3).
- Median mUFC dose: 10 mg bid at week 22; 5 mg bid at month 19.
- 14 of 16 patients were still on treatment at month 19.
- Two patients discontinued before month 19 (AEs: n=1 [increased ACTH and pituitary tumor enlargement]; withdrawal consent: n=1).

**Efficacy**

**Cortisol Levels**

- Mean mUFC decreased from study baseline to <ULN by week 6 and remained in the normal range through to month 19 (Figure 1).

**Clinical Signs of Cushing’s Disease**

- Numerical reductions were seen in mean weight and BMI from baseline to month 19 (Table 2).

**CONCLUSIONS**

- Olsodrostat led to rapid and sustained decreases in mean mUFC and serum cortisol levels, first seen within 1–2 weeks of treatment.
- Normal mUFC levels were maintained up to 19 months in most patients who entered the extension; no patients experienced exacerbation.

**REFERENCES**


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