Presenting author: Richard Feelders (r.feelders@erasmusmc.nl)

PMON162

Osilodrostat provides sustained clinical benefits and improves health-related quality of life in patients with Cushing's disease: Results from the Phase III LINC 4 study

*Richard A Feelders,[1] *Mônica Gadelha,[2] *Marie Bex,[3] *Przemysław Witek,[4] *Zhanna Belaya,[5] *Yerong Yu,[6] *Adina F Turcu,[7] *Anthony P Heaney,[8] *Richard J Auchus,[7] *Andrea Piacentini,[9] *Alberto M Pedroncelli,[10] *Peter J Snyder[11]

[1]Erasmus Medical Center, Rotterdam, Netherlands; [2]Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; [3]University Hospitals Leuven, Leuven, Belgium; [4]Medical University of Warsaw, Warsaw, Poland; [5]Endocrinology Research Centre, Moscow, Russia; [6]West China Hospital of Sichuan University, Chengdu, China; [7]University of Michigan, Ann Arbor, MI, USA; [8]University of California, Los Angeles, CA, USA; [9]Recordati SpA, Milan, Italy; [10]Recordati AG, Basel, Switzerland; [11]University of Pennsylvania, Philadelphia, PA, USA

Introduction

- As a consequence of chronic hypercortisolism, Cushing's disease is associated with cardiovascular morbidity and mortality, as well as impaired QoL[1]
- Osilodrostat, a potent oral 11β-hydroxylase inhibitor, normalized mUFC and improved clinical parameters of hypercortisolism and QoL during the 48-week core phase of the Phase III LINC 4 study (NCT02697734)[2]
- **We report here the long-term effects of osilodrostat on cardiovascular and metabolic-related parameters, physical manifestations of hypercortisolism, and QoL following an optional extension phase to LINC 4**

CONCLUSIONS

- **Improvements in cardiovascular and metabolic-related parameters that occurred during the core phase were maintained during long-term osilodrostat treatment, including reductions in blood pressure, glycemic parameters, weight and waist circumference, and total cholesterol**
- **Physical manifestations of hypercortisolism improved or remained stable from baseline to week 48 and end of treatment in most patients**
- **Improvements in patient-reported outcomes, such as CushingQoL and BDI-II scores, that were observed during the core phase continued during the extension**
- **Osilodrostat is an effective and well-tolerated long-term treatment that may alleviate disease burden and improve QoL for many patients with Cushing's disease**

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Disclosures

This study was sponsored by Novartis Pharma AG; as of July 12, 2019, osilodrostat is an asset of Recordati AG

*Potential conflict of interest may exist. Refer to the Meeting App

References

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3. Webb SM *et al*. *Eur J Endocrinol* 2008;158:623–30
4. Beck AT *et al*. *J Pers Assess* 1996;67:588–97

Abbreviations

bid, twice daily; BDI-II, Beck Depression Inventory II; BL, baseline; CI, confidence interval; CushingQoL, Cushing's Quality of Life; DBP, diastolic blood pressure; EOT, end of treatment; FPG, fasting plasma glucose; HbA$_{1c}$, glycated hemoglobin; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; mUFC, mean urinary free cortisol; QoL, quality of life; QR, quick response; SBP, systolic blood pressure; SD, standard deviation; UFC, urinary free cortisol

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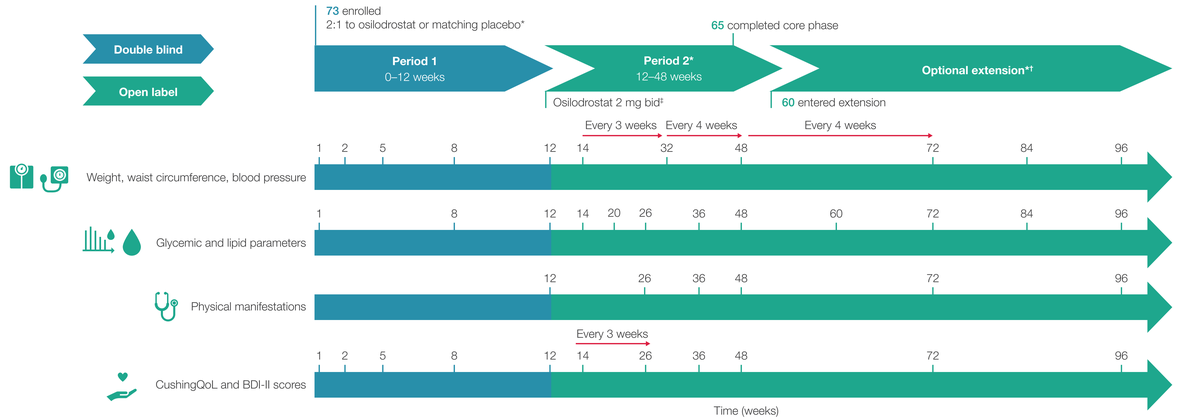
Methods

LINC 4: Phase III study with an initial 12-week, double-blind, randomized, placebo-controlled period followed by open-label treatment until week 48, and an optional extension phase



*Dose increases (starting dose: 2 mg bid), were permitted every 3 weeks to normalize mUFC (maximum dose: 20 mg bid during period 1, 30 mg bid during period 2 and optional extension); dose decreases were permitted at any time for tolerability; †A protocol amendment was implemented in December 2019 that specified that the maximum duration of osilodrostat treatment was 96 weeks; however, at the time of the protocol amendment, some patients had already completed >96 weeks of treatment. The protocol amendment specified that patients enrolled in the optional extension phase were asked to come for an EOT visit within 4 weeks after amendment approval at their site, or by week 96, whichever occurred first. Patients who were still receiving clinical benefit were eligible to join a separate long-term follow-up study (NCT03606408); ‡Patients on <2 mg bid at week 12 were restarted on the same dose

- Physical manifestations of hypercortisolism were assessed locally using frontal and lateral images of the shoulders up and frontal and dorsal images of the trunk; physical manifestations were rated on a semi-quantitative scale: 0=absent; 1=mild; 2=moderate; 3=severe

Results

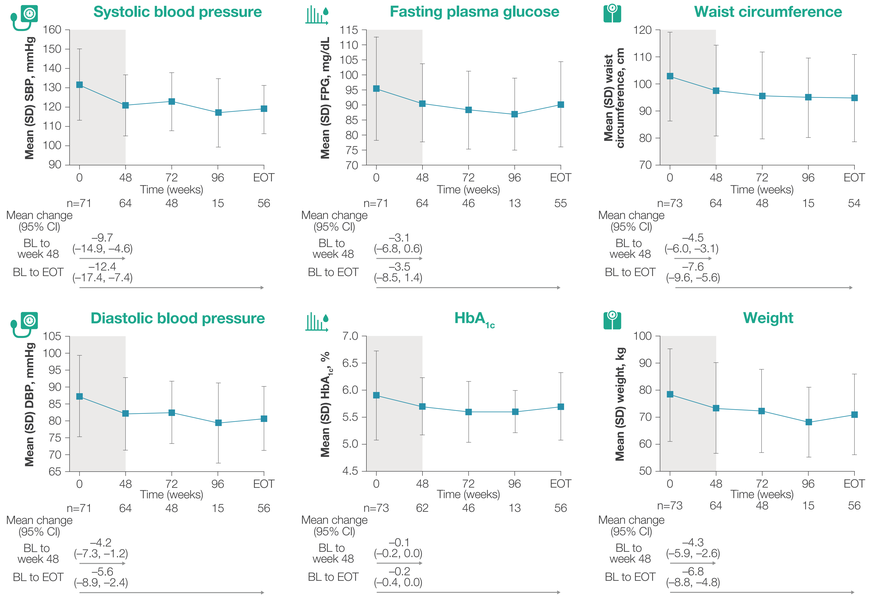
Median (range) osilodrostat exposure: 87.1 (2–127) weeks

Median (IQR) average osilodrostat dose: 4.6 (3.7–9.2) mg/day

98.6% (n=72/73) of patients received ≥1 concomitant medication during the study

mUFC was rapidly normalized and sustained during long-term osilodrostat treatment. See poster RC7.6 for full efficacy and safety results following completion of the LINC 4 extension

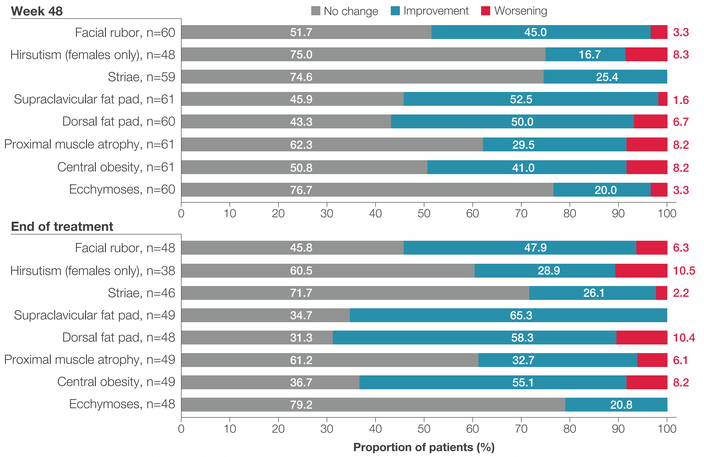
1. Improvements in cardiovascular and metabolic-related parameters observed at week 48 were maintained during long-term osilodrostat treatment



- Scan QR code for data on LDL cholesterol, HDL cholesterol and triglycerides

Shaded areas represent results during the core phase. n is the number of patients with an evaluable assessment at both baseline and the later time point (ie weeks 48, 72, 96 or end of treatment [EOT])

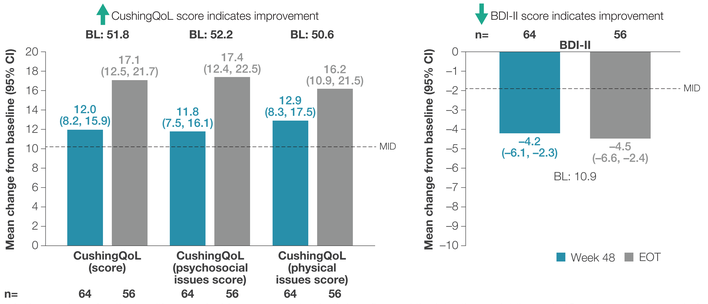
2. Physical manifestations of hypercortisolism improved or remained stable from baseline to week 48 and end of treatment in most patients, with few patients experiencing worsening features



n is the number of patients with an evaluable assessment at both baseline and the later time point (ie week 48 or end of treatment)

- Scan QR code for data on severity of physical manifestations of hypercortisolism at baseline

3. Improvements in patient-reported outcomes (CushingQoL and BDI-II scores) during the core phase were maintained during long-term osilodrostat treatment



n is the number of patients with an evaluable assessment at both baseline and the later time point (ie week 48 or the extension end of treatment [EOT] visit). Dotted line indicates the distribution-based minimal important difference (MID) corresponding to a 10.1-point change from baseline for CushingQoL[2] and a 17.5% reduction in scores from baseline for BDI-II[3]