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Background: Improved patient-reported outcomes (PROs) are increasingly becoming a key treatment objective in acromegaly. Validated PROs were used to assess disease and treatment burden in the MPOWERED phase 3 trial in acromegaly, which also assessed safety and efficacy of oral octreotide capsules (OOC; MYCAPSSA®) compared to injectable SRLs (iSRLs).
Methods: Eligible patients had acromegaly diagnosis, biochemical control of acromegaly (insulin-like growth factor I <1.3 × upper limit of normal; mean integrated growth hormone, <2.5 ng/mL) and ≥6 months' iSRL treatment (octreotide or lanreotide). Eligible patients entered a 26-week Run-in phase to determine the effective OOC dose; responders at week 24 then entered a 36-week randomized controlled treatment (RCT) phase receiving OOC or iSRLs in a 3:2 ratio. The Acromegaly Treatment Satisfaction Questionnaire (Acro-TSQ) is a recently validated tool that includes 27 items in 6 domain scores for PROs in acromegaly.[1] Acro-TSQ data were collected at baseline (reflecting outcomes on iSRLs), end of Run-in (reflecting outcomes on OOC), and end of RCT (OOC or iSRLs).
Results: Of 146 enrolled patients, 92 entered RCT (OOC, N=55; iSRLs, N=37). Acro-TSQ scores at the end of Run-in (26 weeks' OOC treatment) were compared to baseline (iSRLs). In the 92 patients randomized, 3 of 5 Acro-TSQ domains (emotional reaction, treatment convenience, and treatment satisfaction) showed significant improvement at end of Run-in compared to baseline. Injection site interference was not assessed as no injection site reactions were observed with OOC. Other domains showed a nonstatistically significant pattern of improvement at end of Run-in when compared to baseline. Patients randomized to iSRLs in the RCT after receiving OOC in the Run-in (N=37) reported more anxiety (RCT end, 53%; Run-in end, 29%) and frustration (RCT end, 45%; Run-in end, 34%) with iSRLs compared to OOC. Overall treatment satisfaction was higher while receiving OOC (Run-in end, 92%; after receiving iSRLs in RCT, 75%). Breakthrough symptoms were reported more frequently with iSRLs (31%) than OOC (15%) at the end of RCT.
Conclusion: Higher patient satisfaction, convenience and emotional well-being, and improved symptom control based on the newly validated Acro-TSQ PRO reporting tool were observed with OOC compared to iSRLs in patients enrolled in the MPOWERED trial.
[1]Fleseriu M, et al. *Pituitary*. 2020 Aug;23(4):347-358.

Neuroendocrinology and Pituitary

CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Long-Term Control of Urinary Free Cortisol With Osilodrostat in Patients With Cushing's Disease: Final Results From the LINC 2 Study

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Introduction: During the 22-week core LINC 2 study, the oral 11β-hydroxylase inhibitor osilodrostat normalized mean urinary free cortisol (mUFC) in 79% (15/19) of patients with Cushing's disease. This report describes long-term LINC 2 efficacy and safety results following an optional extension. **Methods:** Patients receiving clinical benefit at week 22 could enter the extension (that ran until Oct 22, 2019), continuing the same osilodrostat dose; dose adjustments were permitted based on efficacy and safety. Response rate (mUFC ≤ULN [controlled] *or* mUFC >ULN but ≥50% decrease from baseline [BL; partially controlled]) was assessed over time. Efficacy/safety were assessed for all patients from core BL until study end. **Results:** Of 19 enrolled patients (female:male 14:5; mean [SD] age 36.8 years [8.4]), 16 entered the optional extension and 8 of them remained on treatment until study end. Median (range) osilodrostat exposure was 282 weeks (2-351). Mean mUFC decreased from BL (9.9 x ULN) to ≤ULN by week 4 and remained stable throughout the study. All 19 patients achieved mUFC ≤ULN at least once during the study. At each assessment up to month 70 of the extension phase, 50-88% of ongoing patients were controlled, and up to 18% were partially controlled. Mean percentage change in clinical signs from BL (mean [SD]) to last assessment were: fasting plasma glucose, -10.8% (22.1) (from BL: 105.6 mg/dL [49.2]); HbA_{1c}, -2.1% (9.0) (from BL: 5.7% [0.7]); systolic BP, -3.3% (12.6) (from BL: 132.6 mmHg [11.6]); diastolic BP, -2.0% (10.4) (from BL: 85.0 mmHg [6.5]); BMI, -5.9% (8.8) (from BL: 30.7 kg/m^2 [7.0]). Overall, 9 patients discontinued treatment (n=2 core and n=7 extension), mostly because of AEs or no longer requiring treatment (n=3 each). The most common AEs during the entire treatment period were nausea (n=10), adrenal insufficiency, and headache (both n=9). AEs related to hypocortisolism and adrenal hormone precursor accumulation occurred in 11 (mostly adrenal insufficiency, n=9) and 12 patients (mostly hypertension, n=4), respectively; most were grade 1/2 and managed with dose adjustment/interruption and/or concomitant medication. Mean (SD) plasma ACTH increased from 1.8 x ULN (0.9) at BL to 7.1 x ULN (12.3) at week 22 and 6.9 x ULN (12.6) at last assessment. Mean (SD) 11-deoxycortisol increased from 1.2 x ULN (1.3) at BL to 13.6 x ULN (12.2) at week 22 and 3.6 x ULN (4.2) at last assessment. In females, mean (SD) testosterone increased from 0.8 x ULN (0.4) at BL to 2.4 x ULN (2.1) at week 22 and 1.0 x ULN (0.9) at last assessment. Two patients, both female, reported an AE of hirsutism.

Conclusions: Rapid reductions in mUFC were sustained for up to 6 years of osilodrostat treatment and were accompanied by improvements in clinical signs of hypercortisolism. Osilodrostat was well tolerated, with no new safety signals during long-term treatment.

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CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Medical Treatment Achieves Similar Quality of Life to Surgically Treated Acromegaly Patients in Remission: The QuaLAT Study

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Background: Quality of life (QOL) in acromegaly has been a subject of interest in several published studies; however, there is no consensus on how QOL in patients who require medical treatment after surgery compares with those who achieve remission by surgery only.
Aim: Quality of life after acromegaly treatment (QuaLAT) is a case-control questionnaire-based study with the aim to compare the QOL in those who were treated with surgery only with those who required medical treatment after surgery at a single tertiary centre for acromegaly.
Methods: Patients with acromegaly attending endocrinology clinics were identified via our database. These were matched on the duration of disease into those who underwent surgery and went into disease remission biochemically (Group 1), and those who did not achieve biochemical remission after surgery and therefore required further medical treatment to control the disease (Group 2). Participants were then asked to fill three questionnaires to measure their QOL; Acromegaly Quality of Life Questionnaire (ACROQOL), and two generic questionnaires; 36-Item Short Form Survey (SF36) v2, and Fatigue Severity Scale (FSS).
Results: 20 patients from each group participated in the study. The mean±SD duration of acromegaly (years) was similar in the two groups (9.8±6.9 vs 9.7±6.9 p=0.653). The majority of patients in the medical group were on somatostatin analogues, either alone or in combination (n=14), with four and two patients on cabergoline and pegvisomant alone respectively. There was no difference in QOL scores between groups 1 & 2, as measured by ACROQOL (mean score±SD 54.4±24.8 vs 55.3±26.1 p=0.765), SF36v2 (Physical component score 40.1± 11.1 vs 45.6±12.0 p=0.235; mental component score 41.7±13.0 vs 43.1±16.4 p=0.601), or FSS (mean score±SD 4.4±2.2 vs 4.5±2.0 p=0.985) questionnaires. There was no difference in ages between both groups and there were 75% females in group 1 and 45% in group 2. When compared with healthy controls as reported in the published literature, all three QOL scores were lower in our cohort [1-3].
Conclusions: Medical treatment achieves similar QOL to surgically treated acromegaly patients in remission in the long term. When compared with healthy controls, QOL remains worse in treated acromegaly patients.
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Neuroendocrinology and Pituitary
CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Oral Octreotide Capsules Lowered Incidence and Improved Severity of Acromegaly Symptoms Compared to Injectable Somatostatin Receptor Ligands—Results From the MPOWERED Trial

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Background: Patients with acromegaly may have high symptom burden. The phase 3 MPOWERED trial assessed control of acromegaly by oral octreotide capsules (OOC; MYCAPSSA®) in comparison to injectable somatostatin receptor ligands (iSRLs) in patients responding to both OOC and iSRLs. iSRLs have been first-line medical treatment for patients with acromegaly for decades. OOC are newly approved in the US for patients previously controlled on iSRLs.
Methods: Eligibility criteria for MPOWERED included acromegaly diagnosis, biochemical control of acromegaly (insulin-like growth factor I <1.3 × upper limit of normal; mean integrated growth hormone, <2.5 ng/mL) and ≥6 months' iSRL (octreotide, lanreotide) treatment. Eligible patients entered a 26-week Run-in phase to determine the effective OOC dose; responders at week 24 then entered a