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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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

36-week randomized controlled treatment (RCT) phase receiving OOC or iSRLs. Acromegaly symptom number and severity (mild to severe, 1-3) were collected. Total score was calculated by summating all severity scores (Acromegaly Index of Severity [AIS]). Symptom results were assessed using total AIS score and proportion of patients experiencing individual symptoms.

Results: At beginning of Run-in, average AIS score of 92 randomized patients was 4.52, representative of symptoms experienced while previously receiving iSRLs. After 26 weeks' OOC treatment at end of Run-in, average AIS score was significantly reduced to 3.46 (P<0.001). More than 80% of patients on OOC improved or maintained AIS score during Run-in compared to baseline. Over this 26-week period, there was a significant reduction in extremity swelling (P=0.01) and fatigue (P=0.03). During the RCT, of patients randomized to OOC (n=55), 73% maintained or improved AIS score, and 75% maintained or reduced overall number of active symptoms. In comparison, 68% of those randomized to iSRLs (n=37) maintained or improved AIS score, and 70% maintained or reduced overall number of active symptoms.

Conclusion: Results from MPOWERED show that patients receiving OOC had significant improvement in number and severity of acromegaly symptoms after switching from iSRLs. These findings validate previous results from a phase 3 study of OOC in acromegaly in which patients switching to OOC from iSRLs showed significant reduction in joint pain, extremity swelling, and fatigue.[1]

[1]Melmed S, et al. *JCEM*. 2015;100(4):1699-1708.

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CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Outcome of Petrosal Venous Sampling in Consecutive 68 Patients From a Major Neurosurgical Center in the United Kingdom

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Background: Cushing's disease is a challenging endocrine disorder caused by non-physiological cortisol excess from adrenocorticotropic hormone (ACTH) secreting pituitary adenoma. Inferior petrosal venous sampling (IPSS) is considered the gold standard investigation to differentiate Cushing's disease from ectopic ACTH syndrome. **Methods:** This retrospective study included all patients who underwent IPSS between January 2011 and October 2020 at The National Hospital for Neurology and Neurosurgery in London. Patients demographics, radiological, surgical, endocrinological and, histological data were retrieved. We assessed the accuracy of IPSS in localizing ACTH secreting pituitary adenoma and its concordance with neuroimaging and surgical findings at the time of tumor resection. **Results:** In total 68 patients underwent IPSS, 22 males and 46 females. The median age was 42 years. IPSS was performed prior to primary surgery in 61 patients (90%) and before secondary surgery in 4 patients (6%). Three patients (4%) are awaiting surgery at the time of our study. Fifty-two patients (80%) had positive histology of ACTH expressing adenoma. Four patients (8%) had ectopic ACTH syndrome. The sensitivity of IPSS in predicting Cushing's disease prior to corticotropin-releasing hormone (CRH) stimulation was 91% (95% CI [83% to 97%]) and accuracy of 88% (95% CI [77% to 95%]). The sensitivity of IPSS post CRH administration was 96% (95% CI [87% to 100%]) with accuracy of 86% (95% CI [75% to 93%]). Data on lateralization of pituitary adenoma were available for 63 patients. Prior to CRH stimulation, lateralization was right sided in 35 patients (56%), left sided in 15 (24%), and 13 patients (20%) did not have adequate interpetrosal sinus ACTH ratio. Lateralization post CRH stimulation was right sided in 40 patients (64%), left sided in 20 (32%), and 3 patients (4%) did not achieve adequate ACTH gradient ratio between two sides. Eighteen patients (30%) switched adenoma lateralization between pre and post CRH stimulation. Post CRH IPSS was consistent with neuroradiology in localizing pituitary adenomas in 59% (29 out of 49 patients) and concordant with surgical findings in 41% (25 out of 61 patients). Patients with ectopic ACTH syndrome had negative IPSS at all stages. IPSS procedure failed in 2 patients (3%). No post procedure complications were reported.

Conclusion: IPSS has high sensitivity in diagnosing pituitary driven Cushing's disease with good safety profile. However, the reliability in lateralizing pituitary adenoma is debated. One third of patients in this cohort switched lateralization before and after CRH administration. Studies on monkeys and rats showed that CRH induces coronary vasodilation and reduction in systemic vascular resistance. This suggest that CRH might have vasoactive effect on pituitary blood vessels with subsequent influence on IPS:P ACTH gradient ratio between the two sides.

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CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Pegvisomant as Monotherapy or Combination Therapy in Somatostatin Refractory Acromegaly

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Background: Pegvisomant, a growth hormone antagonist, has been widely used as monotherapy or combination therapy with somatostatin (SST) analogs and/or dopamine agonists in acromegaly poorly controlled by SST analogs. Limited information is available to compare pegvisomant monotherapy, combination with SST analogs or dopamine agonists, and combination of all three agents.

Method: In this retrospective cohort study, we identified 23 patients with SST analog refractory acromegaly who received pegvisomant as monotherapy or in combination with SST analogs and/or dopamine agonists through the Research Patient Data Registry. We divided the patients into four groups: Group 1. pegvisomant alone (n=8);