in most patients (n=12; 85.7%). Of 9 patients with IGF-I ≥1.3 × ULN at sub-study start, 5 (55.6%; 95% CI, 21.2%-86.3%) exhibited IGF-I decreased to predefined responder range (<1.3 × ULN) by week 36. AE incidence and nature with combined treatment were similar to known octreotide safety profile and acromegaly disease burden. There were no serious AEs or AEs leading to discontinuation of either sub-study drug.

Conclusion: We have shown for the first time the benefit of an all-oral combination treatment for acromegaly and avoidance of injection-related burdens. Addition of cabergoline to OOC yielded biochemical control improvement (IGF-I reduction) in patients inadequately controlled with OOC monotherapy. As both combination and OOC monotherapy safety profiles were similar, adjunctive cabergoline may be helpful in patients with acromegaly who do not achieve adequate biochemical control on OOC alone.

[1]Giustina A, et al. *Nat Rev Endocrinol.* 2014;10(4):243-248.

Neuroendocrinology and Pituitary

CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Clinical Correlation to E-cadherin and Granulation Patterns in Corticotroph Tumors

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Corticotroph adenomas, either secretory or silent, are associated with significant disease persistence and/or recurrence. Surgical resection is the first line treatment; however, recurrence rates range from 30 to 60%. Although several clinical parameters (i.e. postoperative cortisol level, tumor invasion) have been reported to predict tumor recurrence, none have high diagnostic accuracy. Granulation pattern classifies corticotroph tumors as densely granulated (DG) or sparsely granulated (SG) types, with the latter usually larger and more aggressively behaving. E-cadherin, a calcium-dependent adhesion molecule strongly expressed in normal pituitary cells, plays a role in epithelial cell behavior, tissue development, and suppresses epithelial-mesenchymal transition. Since loss of E-cadherin expression in sparsely granulated somatotroph pituitary tumors correlates with a more aggressive disease course, we sought to examine correlation between E-cadherin expression and behavior in densely versus sparsely granulated corticotroph tumors. A retrospective chart review of adult patients with corticotroph adenomas, seen at our institution between January 2012 - 2020 yielded 62 patients: 18 (29%) male and 44 female (71%), with median age at diagnosis of 49 years (range 25-82). Inclusion criteria required sufficient tissue for E- cadherin immunostaining (IHC). Microadenomas were identified in 19/62 (31%) patients, and 38/62 (52%) patients had clinical and biochemical findings consistent with excess cortisol secretion. Pre-operative imaging showed that 22/62 (35%) tumors were invasive into surrounding structures. After further classification as to densely granulated (DG) or sparsely granulated (SG) types by ACTH granulation pattern on IHC, 19/56 (34%) adenomas were SG, 37/56 (66%) were DG and 6 were not classified. E-cadherin staining was absent in 7/62 tumors (11%) and diminished in 5/62 (8%) tumors and staining did not correlate with dense versus sparse corticotroph types. Chi-squared analysis found a significant association between tumor size (greater than or less than 1cm) and secretion, with hormonally active more likely tumors to be microadenomas (p=0.004). Microadenomas were exclusively DG tumors (p<0.001). Further analysis did not find correlation between presence or absence of E-cadherin expression and tumor invasion into adjacent structures, or recurrence. In summary, the data suggests that, unlike somatotroph corticotroph adenomas for recurrence or invasion, nor does it correlate strongly with granulation status.

Neuroendocrinology and Pituitary

CLINICAL TRIALS AND STUDY UPDATES IN NEUROENDOCRINOLOGY AND PITUITARY

Design of the ForesiGHt Trial: A Multicenter, Randomized, Placebo- and Active-Controlled Trial to Compare Once-Weekly TransCon hGH (lonapegsomatropin) to Placebo and Daily Somatropin in Adults With Growth Hormone Deficiency (GHD)

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BackgroundAdult GHD results from insufficient growth hormone (GH) secretion from the anterior pituitary gland and may represent either a continuation of childhood-onset GHD or GHD acquired during adulthood. Clinically, adult GHD is associated with central adiposity, decreased lean muscle mass, increased fat mass, decreased bone mineral density, and reduced quality of life. Current standard of care consists of GH replacement via daily injections.

Lonapegsomatropin is a long-acting prodrug of somatropin (hGH), designed to deliver unmodified hGH with a weekly exposure profile. Lonapegsomatropin consists of somatropin that is transiently bound to a carrier via a proprietary TransCon Linker. The carrier extends the duration of somatropin in the circulation through a shielding effect that minimizes renal excretion and receptor-mediated clearance of the prodrug. At physiologic conditions, lonapegsomatropin releases fully active, unmodified somatropin via autocleavage of the linker in a controlled manner.

The safety and efficacy of lonapegsomatropin have previously been evaluated in two phase 3 trials and one long-term extension trial in pediatric GHD. Changes in body