

OR23-07: Results from the Phase 3, Randomized, Double-Blind, Placebo-Controlled CHIASMA OPTIMAL Study of Oral Octreotide Capsules in Adult Patients with Acromegaly

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Many patients taking long-acting somatostatin receptor ligand (SRL) injections as first-line medical therapy in acromegaly report limitations, including ongoing disease symptoms especially near injection cycle end and injection site pain. Oral octreotide capsules may provide an alternative to monthly injections.

The phase 3 Octreotide capsules versus Placebo Treatment In MultinationAL centers (OPTIMAL) study assessed efficacy and safety of oral octreotide capsules in patients with acromegaly controlled on injectable SRLs. A multinational, randomized, placebo-controlled study was conducted in 56 adult patients with active acromegaly. Eligible patients were ≥ 18 years of age, had evidence of active disease ($\text{IGF-I} \geq 1.3 \times \text{ULN} \geq 3$ months after last pituitary surgery), and an average $\text{IGF-I} \leq 1.0 \times \text{ULN}$ on a stable dose of SRL injections (octreotide or lanreotide). At baseline (1 month following the last injection), patients were randomized to receive octreotide capsule or placebo (28 per group) for 36 weeks, followed by an optional open-label oral octreotide extension. The primary endpoint was proportion of patients maintaining biochemical response, defined as $\text{IGF-I} \leq 1.0 \times \text{ULN}$ (2-value average at weeks 34 and 36). Secondary endpoints included need for rescue with injectable SRLs, GH response ($\text{GH} < 2.5$ ng/mL), and time to loss of IGF-I response ($\text{IGF-I} > 1.0$ and $\geq 1.3 \times \text{ULN}$ for 2 consecutive visits). Safety and tolerability were assessed. The primary endpoint was met, as 58% of patients receiving octreotide capsules maintained IGF-I response vs 19% receiving placebo ($P=0.008$). Mean IGF-I levels in patients receiving octreotide capsules were within the reference range at treatment end ($0.97 \times \text{ULN}$) vs patients receiving placebo ($1.69 \times \text{ULN}$). All secondary endpoints were met. Of patients receiving octreotide capsules, 75% completed 36 weeks without need for rescue therapy. However, 68% of the placebo group required rescue therapy. GH response was maintained at week 36 in a significantly larger proportion of patients receiving octreotide capsules than placebo (78% vs 30%; $P=0.001$). Median time to loss of IGF-I response was not reached by the end of the study for patients receiving octreotide capsules vs 16 weeks for the placebo group ($P < 0.0001$). Five patients in the placebo group had IGF-I levels in the reference range at the end of 36 weeks. Only 2 (7% of placebo group) did not meet loss of response criteria anytime throughout the study. Octreotide capsules were safe and well tolerated; no new/unexpected safety signals were observed. Most patients (55/56) experienced at least one treatment emergent adverse event; most were mild or moderate in intensity.

Overall, 90% of patients who completed the trial on octreotide capsules opted to enter the open label extension phase. These phase 3 data demonstrate octreotide capsules to be potentially safe and effective for the treatment of adults with acromegaly.