

OR18-01: Effect of Teprotumumab on Proptosis Reduction Across Various Demographic Sub-Groups

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Introduction: Teprotumumab, an insulin-like growth factor 1 receptor inhibitory monoclonal antibody, was recently shown to significantly reduce proptosis in patients with active, moderate-to-severe thyroid eye disease (TED) in phase 2 and phase 3 clinical trials.^{1,2} Prior analyses have demonstrated a combined trial proptosis response (≥ 2 mm reduction) rate of 77.4% in the teprotumumab group and 14.9% in the placebo group after 24 weeks of therapy ($p < 0.001$).³ The current analysis was performed to investigate whether or not patient demographic characteristics influence the teprotumumab proptosis response.

Methods: Data from two 24-week randomized, double-masked, placebo-controlled, parallel-group, multicenter studies (Phase 2 [NCT01868997], Phase 3 [NCT03298867]) were combined. All patients had active TED associated with Graves' disease. The study eye designated at baseline manifested more severe TED and a clinical activity score of > 4 . Subjects were divided into subgroups based on gender, smoking status, and age at baseline (younger: < 65 , older: ≥ 65). The percentage of proptosis (≥ 2 mm) responders and proptosis change from baseline were examined in each of these subgroups. Because most of both teprotumumab (85%) and placebo (87%) subjects were white, there were insufficient numbers of subjects to examine the effect of race on the teprotumumab proptosis response. All analyses were performed on the intent-to-treat (ITT) population using data from the study eye.

Results: A total of 171 patients comprised the population from the two studies. Eighty-four and 87 patients were randomized to the teprotumumab and placebo groups, respectively, and the treatment groups had balanced baseline characteristics. At week 24, significantly more teprotumumab than placebo patients were proptosis responders in all examined subgroups (male: 73.1% vs. 5.0%, female: 79.3% vs. 17.9%, smokers: 70.0% vs. 23.1%, non-smokers 79.7% vs. 11.5%, younger: 76.1% vs. 16.2%, older: 84.6% vs. 7.7%; all $p < 0.001$). In continuous variable analyses, the mean proptosis reduction from baseline was also significantly greater at week 24 in teprotumumab-treated patients than placebo patients (male: -3.34 vs. -0.07 mm, female: -3.10 vs. -0.42 mm, smokers: -2.99 vs. -0.72 mm, non-smokers: -3.20 vs. -0.31 mm, younger: -3.10 vs. -0.39 mm, older: -3.55 vs. -0.22 mm; all $p < 0.001$).

Conclusion: Teprotumumab was effective across subgroups of age, gender, and smoking status in the pooled 24-week clinical trials.

Reference: 1. Smith TJ, et al. *N Engl J Med* 2017;376:1748-1761. 2. Douglas RS, et al. AACE 2019 late-breaking abstract. 3. Kahaly GJ, et al. *Thyroid* 2019;29(Suppl1):A-1 [abstract].