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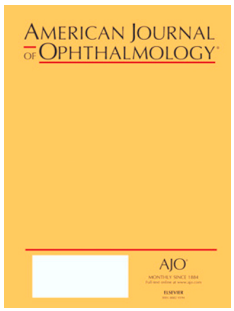

Efficacy of tocilizumab in patients with moderate to severe corticosteroid resistant Graves´ orbitopathy: A randomized clinical trial

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ABSTRACT

Objective: To demonstrate the efficacy of the anti- interleukin-6 receptor monoclonal antibody tocilizumab in patients with moderate to severe corticosteroid resistant Graves´ orbitopathy (GO).

Design: Double-masked randomized clinical trial

Setting and Participants: Thirty-two adults with moderate to severe corticosteroid-resistant GO from ten medical centers in Spain were randomized (1:1)

Intervention: Randomization to either 8 mg/kg body weight tocilizumab or placebo administered intravenously at weeks 0, 4, 8, and 12, and follow-up for an additional 28 weeks.

Main Outcomes and Measures: The primary outcome was the proportion of patients with a change from baseline to week 16 of at least 2 in the clinical activity score (CAS).

Results: The primary outcome was met by 93.3% (95% confidence interval [CI] 70.1%-98.8%) of the patients receiving tocilizumab and 58.8% (36%-78.3%) receiving placebo (P=.04; odds ratio, 9.8 [CI 1.3-73.2]). A significant difference was also observed in the proportion of patients achieving a CAS< 3 (86.7% [CI 62.1%-96.2%] vs. 35.2% [CI 17.3%-58.7%], P=.005; OR 11.9 [CI 2.1-63.1]) at week 16. Additionally, a larger proportion of patients with improvement in the European Group on GO proposed composite ophthalmic score at week 16 (73.3% [CI 48%-89.1%] vs 29.4% [CI 13.2%-53.1%]; P=.03), and exophthalmos size change from baseline to week 16 (-1.5 mm [-2.0- 0.5] vs. 0.0 mm [-1.0.5]; P=.01) were seen with tocilizumab. One patient experienced a moderate increase in transaminases at week 8; another had an acute pyelonephritis at week 32 in the tocilizumab-treated group.

Conclusion: Tocilizumab offers a meaningful improvement in activity and severity in corticosteroid-resistant GO. This trial justifies further studies to characterize the role of tocilizumab in GO