



## Editorial

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### ROLE OF TOCILIZUMAB IN MANAGING THYROID EYE DISEASE

**T**hyroid eye disease (TED), or thyroid-associated ophthalmopathy (TAO), is the most common cause of orbital disease-related proptosis in adults and remains a cause of visual impairment worldwide. It is an autoimmune orbital inflammatory disorder associated with thyroid dysfunction, primarily Graves' disease (90%) and Hashimoto's thyroiditis (3%). TAO is an autoimmune condition in which inflammation causes swelling of the orbital fat and extraocular muscles. Its pathogenesis involves orbital fibroblast activation, excessive hyaluronic acid, adipogenesis, extraocular muscle enlargement, and orbital tissue remodelling. These changes manifest clinically as proptosis, diplopia, and corneal exposure. In severe cases, they may progress to dysthyroid optic neuropathy (DON). These manifestations impair patients' visual function, appearance, and quality of life, requiring effective, timely treatment.

Characteristically, tocilizumab is a monoclonal antibody that targets and blocks **Interleukin-6 (IL-6) receptors**. IL-6 is a key protein driving the inflammatory cascade and tissue swelling in the orbit. **Tocilizumab is a second-line treatment** used for active, moderate-to-severe **Thyroid-Associated Ophthalmopathy (TAO)**, also known as Thyroid Eye Disease (TED). It is usually reserved for patients who do not respond to or cannot tolerate standard corticosteroid therapy. Improvements in the Clinical Activity Score (CAS) and thyrotropin receptor antibody (TRAb) levels throughout the therapy are the primary outcome. The ophthalmic score, including CAS, proptosis, eyelid retraction, and diplopia, was used to evaluate secondary improvement in TAO.

A study of 54 steroid-resistant TED patients found that 74% achieved an absolute CAS response (CAS = 0 or 1) after the 4th dose of tocilizumab (week 16), and 55% (23/42) achieved a TRAb response. In CAS, 90.9% of patients (40/44) achieved a response (reduction > 2 points) after the first dose of tocilizumab (week 4). Measurements of proptosis (reduction  $\geq 2$  mm in 78% of patients, 42/54) and eyelid retraction (reduction  $\geq 2$  mm in 75% of patients, 33/44), and the prevalence of diplopia (improvement in 68% of patients, 19/28) were significantly reduced after the last dose of tocilizumab. A course of at least 4 months (one monthly dose) of tocilizumab therapy provides a significant benefit to patients with active moderate-to-severe steroid-resistant GO.

A study describes the efficacy of tocilizumab in patients with Graves' orbitopathy resistant to or dependent on steroids and compares it to rituximab-treated patients. Graves' orbitopathy response was considered a decrease of at least 2 points on the CAS. Twenty-one patients were included: seven were treated with tocilizumab and 14 with rituximab. The primary results were satisfactory, achieved in all patients (100%) on tocilizumab and 64% of patients on rituximab ( $p = .17$ ). Mean change in CAS was consistent with a decrease of  $3.3 \pm 0.5$  points in patients on tocilizumab versus  $2.5 \pm 1.9$  in patients on rituximab ( $p = .07$ ). One patient on tocilizumab (14%) and 4 patients (29%) on rituximab experienced significant relapse during the follow-up. Relapse-free survival did not differ significantly between patients on tocilizumab ( $10.8 \pm 4$  months) and rituximab ( $17.88 \pm 3.66$  months). Tocilizumab significantly improved CAS, visual acuity, diplopia, and proptosis, as did rituximab.

The response to systemic corticosteroid therapy is not satisfactory because up to 55% of patients show an incomplete response, and relapses are commonly observed. Tocilizumab (TCZ), a monoclonal antibody that targets the interleukin-6 receptor, is an effective second-line therapy for active, moderate-to-severe steroid-resistant TED with clinically significant improvements in ophthalmic score response, CAS, proptosis, and quality of life, with a generally acceptable safety profile.

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