



HYPERTHYROIDISM

Tocilizumab treatment for Graves' eye disease

BACKGROUND

Graves' eye disease (also called Graves' ophthalmopathy or orbitopathy or thyroid eye disease) is a condition associated with the autoimmune hyperthyroid disorder known as Graves' disease. The inflammation in Graves' disease can affect the eyes in patients and can cause symptoms ranging from mild eye irritation to severe eye bulging and double vision. In severe cases, it can be associated with loss of sight. Severe Graves' disease often leads to eye surgery to correct the bulging and/or double vision. Medical treatment options are limited. High dose corticosteroids alone or in combination with radiation treatments can be used to treat moderate to severe Graves' eye disease, but are associated with significant adverse health effects. Side effects of corticosteroids, particularly the higher doses used in this condition, include weight gain, elevated blood glucose or diabetes, high blood pressure, difficulty sleeping and mood changes. Therefore, researchers have sought to find alternative treatments. Cells surrounding the eye (orbital fibroblasts) secrete an inflammatory protein named interleukin-6 (IL-6) which is thought to be involved in the development of Graves' eye disease. In this study, the investigators researched whether interfering with the function of this protein using an antibody against IL-6 would improve eye symptoms in patients with Graves' eye disease.

THE FULL ARTICLE TITLE:

Perez-Moreiras JV et al 2018 Efficacy of tocilizumab in patients with moderate-to-severe corticosteroid-resistant graves orbitopathy: a randomized clinical trial. *Am J Ophthalmol* 195:181–190. Epub 2018 Aug 4. PMID: 30081019.

SUMMARY OF THE STUDY:

These investigators recruited 32 patients with moderate to severe Graves' eye disease that had not previously responded to corticosteroid treatment from 10 medical centers in Spain. Patients were randomized to receive either placebo or the IL-6 receptor monoclonal antibody

tocilizumab. Patients received either tocilizumab or placebo intravenously every 4 weeks for a total of 12 weeks and then were followed for improvement in eye symptoms for 28 weeks. A 10-point clinical activity score (CAS) was the primary method used to rate patient eye symptoms. The CAS measured a number of different eye symptoms including eye pain, redness, swelling, impairment in eye movements, bulging of eyes and vision. Patients also filled out questionnaires to evaluate their eye pain and quality of life. The primary outcome was the percentage of patients that had an improvement of 2 or more points in their CAS assessment.

More patients receiving tocilizumab (93.3%) compared to the placebo (58.8%) group demonstrated a 2 or more point improvement in CAS. Other tests of eye disease symptoms also showed more improvement in the tocilizumab treated patients compared to placebo. Tocilizumab was associated with significantly more adverse effects than the placebo. A total of 93 adverse events were reported in 27 patients, only 2 events (abnormal liver test and kidney infection) were considered serious and both of these occurred in patients treated with tocilizumab. At the study conclusion (40 weeks), significantly more patients treated with tocilizumab (80%) experienced greater than 1 adverse event than patients treated with placebo (41%) but none of the participants withdrew from the study due to an adverse event.

WHAT ARE THE IMPLICATIONS OF THE STUDY?

This study provides clinical experience with a potentially promising new medication for the treatment of moderate to severe Graves' eye disease in patients who do not respond to first line therapy with corticosteroids. Tocilizumab treatment was more effective than placebo in improving eye symptoms in patients with difficult to treat Graves' eye disease. Future studies in larger groups of patients are needed to confirm these findings.

—Whitney Woodmansee MD





HYPERTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Graves' Disease: <https://www.thyroid.org/graves-disease/>

Graves' Eye Disease: <https://www.thyroid.org/graves-eye-disease/>

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>

ABBREVIATIONS & DEFINITIONS

Graves' disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Graves' eye disease: also known as Graves ophthalmopathy or orbitopathy or thyroid eye disease. Graves' eye disease is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis. It includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

Immune system: a system of organs, tissues, and cells in our body that has the role to recognize potentially harmful foreign substances and organisms as well as abnormal body cells and produce antibodies to destroy these factors.

Glucocorticoids: general antiinflammatory and immunosuppressive drugs that are commonly used for the treatment of many autoimmune diseases associated with inflammation

Tocilizumab: a monoclonal antibody drug that is administered intravenously and blocks the activity of the inflammatory protein interleukin-6 (IL-6)

CAS: Clinical Activity Score, a scoring system used to evaluate patients with Graves' ophthalmopathy, and is based on classical signs of inflammation (pain, redness, swelling and function) and that helps predict which patients will benefit from immunosuppressive treatment

