

CE Credit - Case Report(s) & Topic Review

Teprotumumab Treatment for Thyroid Eye Disease in a Patient with Pre-Existing Hearing Loss: Worth the Risk?

Wyatt Hyke, OD¹, Cheryl Brooke Polinsky, OD², Lisa Schifanella, OD, MS³

CRO (Clinical & Refractive Optometry) Journal

ABSTRACT

Thyroid eye disease (TED) can lead to reduced vision from corneal scarring or optic nerve compression. Other manifestations of thyroid eye disease that can be troubling for TED patients include proptosis, extraocular muscle restrictions and diplopia, soft tissue swelling, dry eye, and conjunctival injection over the extraocular muscle insertions. Intravenous teprotumumab was approved by the Food and Drug Administration (FDA) in 2020 for the treatment of active TED. Teprotumumab can cause potentially permanent severe hearing problems, including hearing loss and tinnitus. For those with preexisting hearing impairment, further hearing loss could have a serious impact on activities of daily living. Herein, we report a case of a patient with known sensorineural hearing loss who uses a hearing aid and chose to receive teprotumumab infusions for his active TED. This case will discuss TED, teprotumumab, and its side effects, including hearing loss, and important considerations for patient education for patients with pre-existing hearing loss who are considering teprotumumab infusions.

CASE REPORT

A 50-year-old African American male presented to the clinic 8 months after his eye examination with a new diagnosis of hyperthyroidism. He stated that his endocrinologist told him he needed an eye exam right away. The patient's chief complaint was that his eyes were "bucking". When asked for clarification, he stated that his eyes "felt like they were trying to close". He also stated that his eyes were bulging, especially the right eye. He reported mild ocular irritation. He denied double vision. His ocular history was significant for dry eye diagnosed 8 months prior. He stated he had not

been using the tear drops or ointment prescribed 8 months earlier. He denied prior ocular surgeries or ocular trauma. His medical history included sleep apnea with Continuous Positive Airway Pressure (CPAP) use, hypertension, hyperthyroidism, and gout.

Best corrected visual acuity was 20/20 in the right eye and 20/20 in the left eye. Extraocular muscle testing, pupil functions, and confrontation visual fields were normal in each eye. There were no extraocular muscle restrictions and there was no afferent pupillary defect. Color vision testing was also normal in each eye. Hertel exophthalmometry results were 25 mm in the right eye and 23 mm in the left eye with a base of 104. Slit lamp examination revealed mild soft tissue edema of the upper and lower eyelids in both eyes, along with exophthalmos of the right eye greater than the left. Both eyes exhibited 1+ inferior superficial punctate keratitis (SPK) and 1+ injection of the bulbar conjunctiva. Intraocular pressures measured 12 mm Hg in the right eye and 13 mm Hg in the left eye. Posterior segment evaluation revealed normal optic nerve head appearance with no edema or pallor in either eye (Figure 1). Maculae were also healthy in appearance. Fundus photography and ocular coherence tomography (OCT) of the optic nerve heads were performed and revealed a healthy peripapillary nerve fiber layer in each eye and no optic nerve edema in either eye. Automated screening visual field testing was performed with unreliable results in both eyes. The patient was educated about TED, including the risk of vision loss and blindness from optic nerve compression or from corneal exposure keratopathy scarring. We initiated treatment for his dry eye with carboxymethylcellulose 0.5% artificial tears four times a day in both eyes and lubricating ophthalmic ointment at bedtime in each eye. We stressed the importance of regular eye exams and continued care with endocrinology.

¹ Resident Optometrist, Tuscaloosa VA Medical Center, Alabama, USA

² Optometrist, Tuscaloosa VA Medical Center, Alabama, USA

³ Optometrist and Residency Supervisor, Tuscaloosa VA Medical Center, Alabama, USA

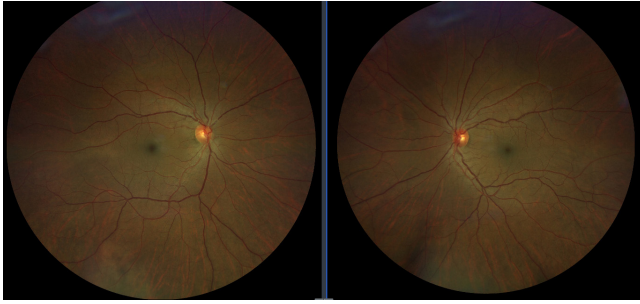


Figure 1: Posterior Segment at initial visit with healthy optic nerve head appearance in each eye

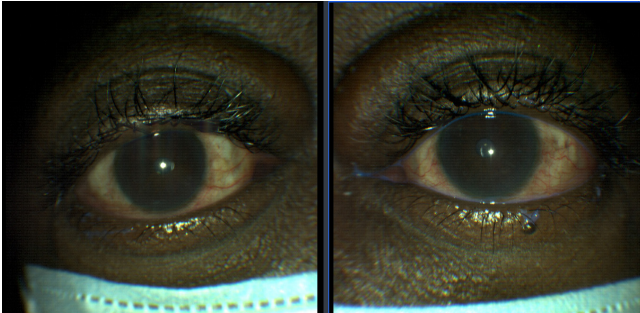


Figure 2: Soft tissue involvement of eyelids with proptosis in the right eye greater than the left eye, at initial visit.

Over the course of the next four months, the patient began to develop worsening proptosis in the right eye, greater than the left, worsening soft tissue swelling of his eyelids, and increased SPK OS (trace superficial punctate keratitis in the right eye, but 2+ inferior superficial punctate keratitis in the left eye) (Figure 2). During this time, the patient's endocrinologist prescribed methimazole to inhibit the production of T3 and T4 hormones. The patient was greatly bothered by his symptoms of "bucking" and irritation and was very dissatisfied with the appearance of the soft-tissue swelling and proptosis. He reported diplopia but could not specify in which direction the images were separated and there were no muscle restrictions on testing. The patient was highly motivated to begin teprotumumab infusions. We referred the patient to an ophthalmologist who proposed a trial of IV steroids. The patient declined, stating that he had been on oral steroids earlier in the year and they had not helped his eyes. He was also concerned about the possible side effects of steroids, including the risk of elevated blood pressure, elevated blood sugar, and anger/psychosis. The patient continued to be highly motivated to receive teprotumumab, and we referred him to an oculoplastic specialist. The specialist noted "burning, tearing, proptosis, diplopia, redness, irritation," resulting in a Clinical Activity Score (CAS) >6. The specialist ordered a 10/mg/kg teprotumumab initial dose followed by 20 mg/kg every 3 weeks for 7 additional infusions. The patient came to our clinic to let us know about the order for the infusions and asked us to set them up for him. We educated the patient about the potential side effects of teprotumumab, including hearing loss, muscle spasms, loss of taste, hair loss, and tiredness/weakness. The patient stated that he

had hearing loss and used hearing aids. He indicated that he was concerned about going deaf and was not sure he wanted to proceed. We contacted the specialist, who wrote a letter recommending proceeding with teprotumumab, with close monitoring of the patient's hearing, and discontinuing teprotumumab if progressive hearing loss occurred. He further noted that if the risk was unacceptable to the patient, the patient could stop the treatment. The patient chose to monitor without teprotumumab.

He presented four months later (eight months after his first exam with us for TED) with complaints of tearing for 3 weeks, especially in the mornings. He stated he had not used the 0.5% carboxymethylcellulose tear drops or the lubricating ophthalmic ointment in 2 months. Of note, the patient reported using a CPAP nightly and smoking five cigars a week. The patient also complained of sensitivity to light and requested sunglasses. Corrected visual acuity was 20/20-2 in each eye. Red cap test revealed no desaturation in either eye. Color vision testing with D-15 was normal for each eye with no reversals for either eye. Confrontation visual fields were full in each eye. Threshold visual field testing was performed, but was unreliable for each eye. Extraocular muscle testing revealed no restrictions. Cover test through his distance correction was 6 prism diopters exophoria at 6m, and through his near correction was 15 prism diopters exophoria at 40cm. Pupils were normal with no afferent pupillary defect. Optic nerves were healthy with no pallor or swelling. We re-educated about thyroid eye disease including the risk for vision loss/blindness from optic nerve compression and/or corneal disease, the importance of keeping the cornea lubricated, the option for teprotumumab and the potential side effects of teprotumumab including the potential for permanent hearing loss. We initiated carboxymethylcellulose 1% 6x/day OU, lubricating ophthalmic ointment at bedtime OU, and fish oil capsules 2000mg a day by mouth.

A month later (9 months after his initial eye exam for TED), the patient called stating that his eyes were "terrible" and that he wanted to start the teprotumumab infusions. We arranged an audiology examination, which revealed normal hearing in the right ear and mild 3kHz sensorineural hearing loss in the left ear. The audiologist's plan was 3- and 6-month audiograms once infusions began, with the patient to return sooner if changes to hearing or tinnitus began.

The patient received his first infusion of teprotumumab 11 months after his initial examination for TED. He presented to us three weeks after the first infusion and stated that his double vision and dryness had both improved. He stated he only saw double when looking behind. Visual acuity was 20/20 in each eye, and the cover test was ortho in each eye at distance and near through correction. Pupil and confrontation visual fields remained normal. Slit lamp showed 1+ SPK inferiorly right cornea and trace inferior SPK left cornea. Intraocular pressures were 17mm Hg in each eye. Optic nerves remained healthy with no pallor or swelling.

During his teprotumumab treatment, the patient had exams with audiology every 3 months. At the final audiology exam after completion of his 8 teprotumumab infusions, the patient reported that he felt he had experienced a change in his hearing. He reported bilateral tinnitus with no change over time. The audiologist diagnosed “slight/mild sensorineural hearing loss and tinnitus bilaterally. Right ear 1kHz is slightly worse compared to last exam, however, this is within test/retest reliability and not likely due to [teprotumumab] infusions.”

The patient was seen for an eye exam four days after completion of his last infusion. He stated that he was pleased overall with the improvements in his symptoms and how he looked following the infusions (Table 1), but expressed some dissatisfaction that he did not look “all the way normal”. He reported that his eyes were still dry but that he no longer saw double. He reported using 1% carboxymethylcellulose four to six times a day, but he had self-discontinued the lubricating ointment at nighttime. Best corrected visual acuity was 20/20 in each eye. Pupils, extraocular muscle testing, and confrontation visual fields were normal in each eye. Cover test was ortho at distance and near with appropriate correction. Hertel exophthalmometry measured 21 mm in the right eye and 19 mm in the left eye with a base of 107. Slit lamp exam revealed mild soft tissue swelling of the right upper lid and moderate swelling of the left upper lid, along with 2+ inferior SPK right eye and 1+ diffuse SPK left cornea. Intraocular pressures were 18 mm Hg right eye and 19 mm Hg left eye. Posterior segment exam was unremarkable in each eye with no optic nerve head edema or pallor in either eye. We discussed the importance of dry eye treatment and the options of starting topical cyclosporine ophthalmic emulsion and restarting lubricating ophthalmic ointment at bedtime. The patient chose to restart the lubricating ointment but delay the start of cyclosporine.

DISCUSSION

TED patients can present with hyperthyroidism, hypothyroidism, or even euthyroid. In the former (Graves’ Disease), autoantibodies bind to the thyroid hormone receptor, resulting in overexpression. Hypothyroidism stems from a variable-cause reduction in hormone production. Euthyroid has an essentially normal thyroid panel.¹ Graves’ disease patients exhibit an increase in insulin-like growth factor 1 receptors (IGF-1R) at the extraocular muscles, which can result in TED even in euthyroid and hypothyroid patients.¹ TED is often categorized into two phases: inflammatory (with active inflammation and resulting changes) or chronic, noninflammatory once the inflammation has resolved. In TED, thyroiditis causes an excess of immune cells in the orbit. The excess of orbital immune cells causes an increase in IGF-1R expression in Graves’ Disease atypically susceptible tissues. The Graves’ Disease IgG-IGF-1R complex induces IL-16 and RANTES, which are chemoattractants that attract

Table 1: The patient’s presence/lack of TED symptoms and change with teprotumumab.

TED Symptom	Post-infusion with teprotumumab
Lid retraction	Improved
Goldzeiher’s Sign (conjunctival injection)	Improved
Corneal dryness	Non-compliant with smoking and CPAP use; little change
Proptosis	Improved
Diplopia	Improved
EOM Restriction	Not present throughout
Unequal pupil size, dim light	Not present throughout
Swelling of lids	Subjective improvement
Hearing loss	Subjective change within test repeatability
Tinnitus	Longstanding, no change
Hyperglycemia	Not reported
Muscle spasms	Not reported

infiltrating T cells.² Increased IGF-1R expression causes an increase in orbital fibroblasts in the orbit, which in turn recruit glycosaminoglycans into the orbital muscles and fatty tissue.³ Essentially, thyroiditis begets more systemic inflammation, which can manifest as swollen orbital and adjacent tissues. As the soft tissue in and around the orbit swells, the contents, including the globe, may be pushed forward, often first raising the upper lid upwards (lid retraction), which facilitates dryness and corneal scarring, as well as physical compression of the orbit muscles on the optic nerve, proptosis, and restriction of eye movements.³ The inflammatory stage of TED generally lasts 1-2 years, but the range is from 0.5 to 5 years.⁴

Effective treatment methods are essential to address the two avenues of permanent vision loss associated with TED: exposure keratopathy causing corneal scarring and optic nerve compression causing optic nerve atrophy. Treatment options include topical lubricating ophthalmic drops and ointments, topical ophthalmic immunomodulators (such as cyclosporine and lifitegrast), omega-3 fatty acids, moisture goggles, tarsorrhaphy, broad-spectrum anti-inflammatory agents (oral or intravenous steroids), immunomodulators such as teprotumumab, and orbital radiation or orbital decompression in severe and/or time-sensitive cases. The treatment options used depend on the severity of the disease and which parts of the eye are involved.

In 2020, teprotumumab was the first drug of its kind to be approved by the FDA for the treatment of TED.⁵ The medication is a monoclonal antibody that inhibits IGF-

1R by way of inhibiting the IGF-1R-TSH proinflammatory (induction of IL-6 and IL-8) complex in fibrocytes.⁶ Teprotumumab is administered intravenously in a dose of 10mg/kg for the initial dose and 20mg/kg for doses 2-8, with potentially more infusions in severe or persistent cases.⁷ Teprotumumab has been shown to be effective in proptosis reduction, CAS improvement, diplopia, and quality of life as compared to placebo.⁸ Several authors, including Stan et al. and Nie et al., have found that teprotumumab is effective in decreasing orbital volume and in treating soft tissue swelling, proptosis, and lid retraction.^{9,10} Of note, Ugradar et al. found teprotumumab to be effective in proptosis reduction even in non-inflammatory TED, defined in their study as those with elevated orbital IGF-1R with a CAS of 1 or less.¹¹ We observed an improvement in soft tissue swelling and reduction in proptosis in our patient (Figure 3), with a resultant decrease in the risk for exposure keratopathy as well (although one could argue his corneal dryness was also related to his smoking and CPAP use).

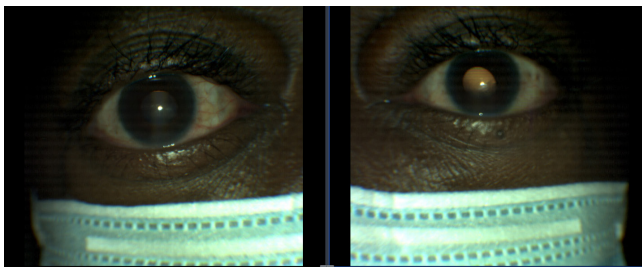


Figure 3: Reduced soft tissue involvement of eyelids with improvement in proptosis and injection of the right eye and left eye following completion of Tepezza.

Because of the potential side effects of teprotumumab and its high cost (over \$18,000 per injection vial as of June 2025), specific guidelines govern its use. TED patients should have an evaluation of their thyroid state (i.e., hyper-, hypo-, or euthyroid) and receive the appropriate endocrine care. Testing for serum antibodies against thyroid-stimulating hormone receptors is considered the gold standard for establishing a Graves' disease diagnosis and is also considered the most reliable laboratory biomarker in differentiating TED and non-TED. A subjective point-based Clinical Activity Score (CAS) composed of seven items is used to demonstrate if TED is active or not, with a score of greater than 4 indicated for insurance coverage according to United Healthcare's guidelines. Another prescribing guideline for teprotumumab is the failure of or contraindication to glucocorticosteroids. Glucocorticosteroids are the traditional first line treatment for TED, as the goal of managing the active-phase inflammation with steroids is generally effective with a 67.44% responder rate.¹² The label for Teprotumumab itself simply states that it is indicated in all thyroid eye disease regardless of activity or duration.¹³

After the failure of or contraindication to steroids, teprotumumab therapy may be the next step. Other options for treatment of the more severe forms of TED include

orbital irradiation and orbital depression. These therapies might be chosen before teprotumumab in cases which demand a more immediate resolution of orbital swelling for the purpose of preserving the optic nerve. A patient is expected to receive only 8 doses of teprotumumab for TED in his or her lifetime.⁸

The risk profile for teprotumumab includes three primary adverse effects, which are thought to be the results of teprotumumab IGF-1R inhibition: muscle spasms, hyperglycemia, and hearing loss. Muscle spasms have been linked directly to a depletion of IGF-1 in the neocortex, and IGF-1 supplementation has been found to alleviate epileptic spasms in trial mice.¹⁴ IGF-1 is abundant in skeletal muscles and IGF increases skeletal muscle uptake of glucose. Bang et al. reviewed studies illustrating the positively correlating relationship between free IGF-1 and hypoglycemic events, and vice versa.¹⁵ Thus, it is believed that teprotumumab results in hyperglycemia because the IGF-1R receptors are no longer binding IGF, a fundamentally insulin-like molecule, and blood sugar reacts accordingly and ceases to be uptaken by muscles. Hearing loss is believed to occur because IGF-1R is involved in cochlear hair cell maintenance and repair by inhibiting hearing cell apoptosis and inducing supporting cell proliferation.¹⁶ Thus, it is believed that the IGF-1R receptor inhibition with teprotumumab leads to an increase in the risk of sensorineural hearing loss (SNHL) in a pathway not dissimilar to age-related hearing loss, which results from the decline of serum IGF-1 and the decrease of cochlear hair cells thereafter.

Depending on the literature cited, the risk for hearing loss varies widely. In the Phase 3 FDA study of teprotumumab, Douglas et al. found that approximately 10% (5 of 42 in the teprotumumab group) suffered hearing loss with resolution.⁷ McGwin et al. noted in their analysis of 940 reported teprotumumab-related adverse events that the drug resulted in a roughly 24-fold increase in risk of hearing loss from baseline.⁵ Sears et al. found in their study of 27 patients that 81.5% had a subjective change in hearing, whether it be from tinnitus (100% resolution), ear fullness (90.9% resolution), or autophony (83.3% resolution)—although only 5 of 11 (45.5%) of patients with subjective hearing loss/decreased word comprehension found resolution.¹⁷ The randomized clinical trials by Douglas et al. and Smith et al. found a 12% incidence of hearing loss (5 patients with disparate etiologies; 100% resolution of each) and 7% incidence of hearing loss (3 patients; 1 with unilateral 16-week post-treatment onset of unilateral hearing loss, 1 with mild bilateral hearing loss that resolved, and 1 with reported tinnitus with a history of tinnitus), respectively.^{7,18} Douglas et al. studied 52 patients and found a 3% incidence of new SNHL with 20% of those with preexisting SNHL experiencing a decline from baseline, with 5 of the 9 resolving.¹⁹ It is unclear why hearing changes sometimes recover post-teprotumumab with a return of IGF-1 and sometimes do not. Hair cells

repair but do not grow anew. To provide a more complete understanding of an individual patient's risk for SNHL, baseline audiology examination with regular audiology follow-ups during the course of teprotumumab treatment are recommended across the literature. Indeed, Douglas et al. performed audiology evaluations prior to treatment, after every other injection, and at the conclusion of treatment in the previously mentioned study.¹⁹

The long-term effectiveness of teprotumumab hinges on the infusions being given during the active inflammatory phase of TED. Basically, teprotumumab treats the active inflammatory stage when the IGF-1R receptor sites are constantly increased due to active TED inflammation. The severity reduction of the finite inflammatory stage (an average of about 2 years) is what causes long term improvement: teprotumumab mitigates the accumulation of orbital fluid, hypertrophy, inflammatory cells, and fibrosis to reduce orbital congestion for the purpose of a better outcome when the post-inflammatory stage is reached. The goal of teprotumumab treatment is to get patients to the finish line of post-inflammatory TED and to a better finish line than they would have otherwise.

Teprotumumab has also been shown to help some patients even when administered in the post-inflammatory stage TED.¹¹ It is believed that even after the inflammatory cascade and increase in IGF-1R expression have, for the most part, subsided, residual IGF-1R elevation remains, thus allowing for some improvement with treatment.¹¹ Cockerham et al. pointed out that TED often has a delayed diagnosis (about 5 years after initial symptoms) and that inactive TED is often symptomatic and affects quality of life.²⁰ Thus, teprotumumab is a valid treatment in either form of TED.

The effectiveness of teprotumumab seems to be durable because of the gains it makes during the active phase of TED. Kahaly et al. found that 19 of 84 teprotumumab patients (versus 6 of 87 placebo patients) reported moderate-to-large improvements in their Grave's orbitopathy questionnaire responses after the infusions, with the majority of patients reporting maintaining post-injection improvement in proptosis (67%), diplopia (69%), and ophthalmic composite outcome (83%) at 51 weeks.²¹

Alternative treatments for TED are being researched. Tocilizumab is an IL-6R antagonist that works by directly reducing interleukin cytokines in inflammatory TED. It is thought that tocilizumab may prove to be more effective for treating proptosis than teprotumumab with a milder side effect profile (mainly liver enzyme alterations and hyperlipidemia), because it does not affect IGF-1R and the cochlear hair cells.²² Rituximab, a monoclonal antibody used to treat non-Hodgkin lymphoma, leukemia, and other autoimmune diseases, is also being studied for the treatment of TED. Rituximab reduces inflammation through its action against CD20 surface antigens by inducing their

removal through antibodies, complement, and apoptosis.²³ Shen et al. found the effects of rituximab against TED to last 4-6 months with a low side effect profile (primarily mild-moderate infusion reactions).²³ Unfortunately, because rituximab depletes all CD20s, a hallmark autoimmune response cell, there is a concern for the development of serious infections with its use.²³

CONCLUSION

Establishing an appropriate treatment plan for TED is imperative to minimize the risk of permanent vision loss. A number of treatment options are available for the management of TED depending on the severity of the condition and which parts of the eye are involved. Teprotumumab treats lid retraction, proptosis, and periorbital soft tissue swelling in active inflammatory TED. Patients considering teprotumumab treatment should be educated about the potential side effects of teprotumumab, including hyperglycemia, muscle spasms, and hearing problems/hearing loss. Reports of the frequency of hearing problems, the type of hearing problems, and the permanency of hearing problems and loss vary. Patients should be questioned about existing hearing loss and made aware of the potential range of hearing problems associated with teprotumumab use. Additionally, referral should be made to an audiologist for baseline testing and subsequent follow-up examinations during the treatment period.

REFERENCES:

1. Bartalena L, Gallo D, Tanda ML, Kahaly GJ. Thyroid eye disease: Epidemiology, natural history, and risk factors. *Ophthalmic Plast Reconstr Surg.* 2023 Dec 1;39(6S): S2-S8. doi: 10.1097/IOP.0000000000002467.
2. Pritchard J, Han R, Horst N, Cruikshank WW, Smith TJ. Immunoglobulin activation of T cell chemoattractant expression in fibroblasts from patients with graves' disease is mediated through the insulin-like growth factor i receptor pathway. *J Immunol.* 2003 Jun 15;170(12):6348-6354. doi: 10.4049/jimmunol.170.12.6348.
3. Ugradar S, Malkhasyan E, Douglas RS. Teprotumumab for the treatment of thyroid eye disease. *Endocr Rev.* 2024 Nov 22;45(6):843-857. doi: 10.1210/edrev/bnae018.
4. Bothun ED, Scheurer RA, Harrison AR, Lee MS. Update on thyroid eye disease and management. *Clin Ophthalmol.* 2009;3:543-551. doi: 10.2147/ophth.s5228.
5. McGwin G Jr, Owsley C, Vicinanzo M. Teprotumumab-related hearing loss: A large-scale analysis and review of voluntarily reported patient complaints to the Food and Drug Administration (FDA). *Ophthalmic Plast Reconstr Surg.* 2024 Nov-Dec;40(6):639-642. doi: 10.1097/IOP.0000000000002668
6. Chen H, Mester T, Raychaudhuri N, et al. Teprotumumab, an IGF-1R blocking monoclonal antibody inhibits TSH and IGF-1 action in fibrocytes. *J Clin Endocrinol Metab.* 2014 Sep;99(9): E1635-E1640. doi: 10.1210/jc.2014-1580.
7. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. *N Eng J Med.* 2020 Jan 23;382(4):341-352. doi: 10.1056/NEJMoa1910434.
8. Douglas RS, Wang Y, Dailey RA, et al. Teprotumumab in clinical practice: recommendations and considerations from the OPTIC trial investigators. *J Neuroophthalmol.* 2021 Dec 1;41(4):461-468. doi: 10.1097/WNO.0000000000001134.

9. Nie T, Lamb YN. Teprotumumab: A Review in Thyroid Eye Disease. *Drugs*. 2022 Nov;82(17), 1663–1670. doi: 10.1007/s40265-022-01804-1.
10. Stan MN, Krieger, CC. The Adverse Effects Profile of Teprotumumab. *J Clin Endocrinol Metab*. 2023 Aug 18;108(9), e654–e662. doi: 10.1210/clinem/dgad213.
11. Ugradar S, Shi L, Wang Y, Mester T, Yang H, Douglas RS. Teprotumumab for non-inflammatory thyroid eye disease (TED): Evidence for increased IGF-1R expression. *Eye (Lond)*. 2021 Sep;35(9), 2607–2612. doi: 10.1038/s41433-020-01297-w.
12. Langericht J, Kramer I, Kahaly GJ. Glucocorticoids in Graves' orbitopathy: mechanisms of action and clinical application. *Ther Adv Endocrinol Metab*. 2020 Dec14;11:2042018820958335. doi: 10.1177/2042018820958335.
13. Horizon Therapeutics. Tepezza: highlights of prescribing information; 2025.
14. Ballester-Rosado CJ, Le JT, Lam TT, Anderson AE, Frost JD, Jr, Swann JW. IGF-1 impacts neocortical interneuron connectivity in epileptic spasm generation and resolution. *Neurotherapeutics*. 2025 Jan; 22(1), e00477. doi: 10.1016/j.neurot.2024.e00477.
15. Bang P, Polak M, Bossowski A, et al. Frequency and predictive factors of hypoglycemia in patients treated with rhIGF-1: Data from the Eu-IGFD registry. *J Clin Endocrinol Metab*. 2024 Dec 21;109(1): 46–56. doi: 10.1210/clinem/dgad479.
16. Yamahara K, Yamamoto N, Nakagawa T, Ito J. Insulin-like growth factor 1: A novel treatment for the protection or regeneration of cochlear hair cells. *Hear Res*. 2015 Dec;330(Pt A):2–9. doi: 10.1016/j.heares.2015.04.009.
17. Sears CM, Azad AD, Amarikwa L, et al. Hearing dysfunction after treatment with teprotumumab for thyroid eye disease. *Am J Ophthalmol*. 2022 Aug;240, 1–13. doi: 10.1016/j.ajo.2022.02.015.
18. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Eng J Med*. 2017 May 4;376(18):1748–1761. doi: 10.1056/NEJMoa1614949.
19. Douglas RS, Parunakian E, Tolentino J, et al. A prospective study examining audiometry outcomes following teprotumumab treatment for thyroid eye disease. *Thyroid*. 2024 Jan;34(1), 134–137. doi: 10.1089/thy.2023.0466.
20. Cockerham K, Smith TJ, Conrad E, Holt RJ. SAT466 inactive thyroid eye disease patient journey. *J Endocr Soc*. 2023;7(Suppl 1), bvad114.1940. <https://doi.org/10.1210/jendso/bvad114.1940>
21. Kahaly GJ, Douglas RS, Holt RJ, Sile S, Smith TJ. Teprotumumab for patients with active thyroid eye disease: a pooled data analysis, subgroup analyses, and off-treatment follow-up results from two randomised, double-masked, placebo-controlled, multicentre trials. *Lancet. Diabetes Endocrinol*. 2021 Jun;9(6), 360–372. doi: 10.1016/S2213-8587(21)00056-5.
22. Duarte AF, Xavier NF, Sales Sanz M, Cruz AAV. Efficiency and safety of tocilizumab for the treatment of thyroid eye disease: A systematic review. *Ophthalmic Plast Reconstr Surgery*. 2024 Jul-Aug;40(4), 367–373. doi: 10.1097/IOP.0000000000002573.
23. Ostrowski RA, Bussey MR, Shayesteh Y, Jay WM. Rituximab in the treatment of thyroid eye disease: A review. *Neuro-ophthalmology*. 2015 Jun 17; 39(3), 109–115. <https://doi.org/10.3109/01658107.2015.1039140>