A Guide to Thyroid and Thyroid Eye Disease

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Disclosures

Has a relevant financial relationship with

Sanofi - Speaker
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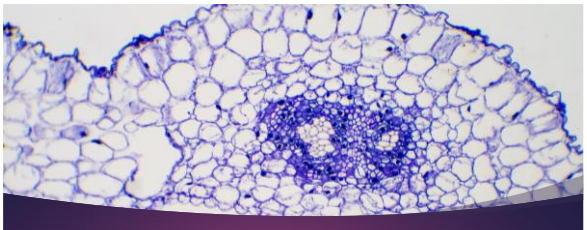

Thyroid Eye Disease

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Incidence of Thyroid eye Disease

	Men	Women
Incidence rate	2.9 cases per 100,000	16 cases per 100,000
Peak age range	45 to 49 years and 65 to 69 years[1]	40 to 44 years and 60 to 64 years[1]

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Thyroid Eye Disease (TED) vs Graves disease

TED vs. Graves' Disease

- TED and Graves' Disease are not synonymous. TED may coexist, precede, or follow Graves' Disease[2]
- TED can exist without hyperthyroidism[1,2,3]

Hyperthyroidism, TED & Graves' Disease

- TED not directly related to high serum thyroid concentrations[4]
- However, euthyroid patients with Graves' Disease tend to have less severe TED[4]

Bartley, G.B. *Trans Am Ophthalmol Soc.* 1994; 92: p. 477-588. 2. Eckstein AK et al. *Br J Ophthalmol.* 2009; 93(8): p. 1052-1056. 3. Leo M et al. *Thyroid.* 2015; 25(3): p. 347-351. 4. Gwinup G et al. *JAMA.* 1982; 247(15): p. 2135-2138

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Risk factors for TED

Risk factors for the development and progression of TED[2]

Nonmodifiable Factors	Modifiable Factors
Age • Advanced Aging **Gender** • Women (more frequent) • Men (more severe) **Genetics**	**Environment** • Smoking • Radioactive Iodine Therapy **Thyroid Dysfunction** • Hypothyroidism • Hyperthyroidism

Bartley, G.B. *Trans Am Ophthalmol Soc.* 1994; 92: p. 477-588. 2. Eckstein AK et al. *Br J Ophthalmol.* 2009; 93(8): p. 1052-1056. 3. Leo M et al. *Thyroid.* 2015; 25(3): p. 347-351. 4. Gwinup G et al. *JAMA.* 1982; 247(15): p. 2135-2138

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Thyroid secretion

- Excessive thyroid secretion
  - Fast pulse
  - Palpitations
  - Profuse sweating
  - High blood pressure
  - Irritability/ fatigue/ heat intolerance
  - Weight loss
  - Loss of hair/ changes in hair quality
- Decreased thyroid secretion
  - Weight gain
  - Hoarse voice
  - Thinning hair
  - Tiredness
  - Weight gain/ puffy face
  - Slow heart rate
  - Depression/ memory problems

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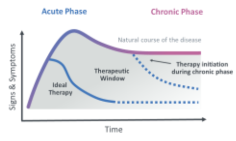
The Natural History of TED



Refined understanding of TED natural course

Acute (active) Stage

- Characterized by inflammation including periorbital chemosis, orbital congestion, and tissue expansion associated with eyelid retraction, proptosis, and diplopia for a variable period up to three years[1-3]

Chronic (inactive) Disease

- Inflammation will subside but the changes may remain and result in permanent damage

1. Bhatti MT, et al. *J Neuroophthalmol*. 2014;34(2):186-197. 2. Bothun ED, et al. *Clin Ophthalmol.* 2009; 3:543-551. 3. Bartalena L, et al. *Endocr Rev.* 2000; 21(2):168-199.

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Clinical Presentation of TED

Conjunctiva and Cornea[1-4]

Figure adapted from Briceño CA, et al. *Int Ophthalmol Clin.* 2013; 53(3): 93-101.

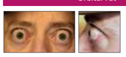
- Chemosis
- Conjunctival redness
- Tearing
- Photophobia
- Foreign body sensation

Eyelid[1-4]

Figure adapted from Briceño CA, et al. *Int Ophthalmol Clin.* 2013; 53(3): 93-101.

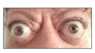
- **Upper eyelid retraction 91%[8]**
- Eyelid swelling
- Pain
- Lagophthalmos
- Exposure keratopathy

Orbital Fat[2-3]



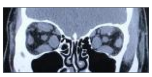
- **Proptosis 60%[8]**
- Pain
- Disfigurement
- Exposure keratopathy
- Vision loss

Extraocular Muscle[2-3]



- Restricted ocular motility
- **Diplopia 51%[9]**
- Pain
- Decreased vision & depth perception

Optic nerve[5-7]



- **Compressive Optic Neuropathy 6-9%[8]**
- Loss of vision
- Impairment of color vision
- Optic disc swelling
- Visual field defect

1. Liaboe C *et al. Thyroid eye disease: an introductory tutorial and overview of disease.* EyeRounds.org. https://webeye.ophth.uiowa.edu/eyeforum/tutorials/thyroid-eye-disease/ Thyroid-Eye-Disease.pdf Published November 18, 2016. Accessed January 10, 2022. 2. Bothun ED *et al. Clin Ophthalmol.* 2009;3:543-551. 3. Bahn RS. *N Engl J Med.* 2010;362(8):726-738. 4. Briceño CA et al. *Int Ophthalmol Clin.* 2013;53(3):93-101. 5. Neigel JM et al. *Ophthalmology.* 1988;95(11):1515-1521. 6. McKeag D et al. *J Ophthalmol.* 2007;91:455-458. 7. Fernandez E et al. *Ann Thyroid Res.* 2016;2:63-65. 8. Bartley GB et al. *Am J Ophthalmol.* 1996;121(4):426-434. 9. Terwee C et al. *Eur J Endocrinol.* 2002;146(6):751-757

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TED Is an Autoimmune Inflammatory Eye Disease

Healthy Eye and Orbital Tissue[3]

In Presence of Moderate to Severe TED[3]

While the exact autoimmune triggers for TED are unknown, autoantibody activation leads to inflammation and tissue expansion/remodeling in the eye[1,2]

Multifactorial causes:

- IGF-1R is overexpressed in TED orbital fibroblasts[4]
- Autoantibodies activate the IGF-1R and TSHR-signaling complex, which stimulates orbital fibroblasts[1] and leads to the release of inflammatory cytokines and hyaluronan production[5-7]
- Once activated, orbital fibroblasts cause inflammation and expansion of tissue, muscle, and fat cells behind the eye[7,8]

1. Smith TJ et al. *Front Endocrinol (Lausanne).* 2016; 7:167. 2. Wang Y et al. *Invest Ophthalmol Vis Sci.* 2014; 55(3): 1735-1748. 3. Horizon Pharma. Events & presentations. https://ir.horizontherapeutics.com/static-files/c153d2c9-fae6-4e3b-ab18-7e8485e2c2d4. Accessed January 10, 2022. 4. Tsui S, et al. J Immunol. 2008;181:4397-4405. 5. Pritchard J, et al. J Immunol. 2003;170:6348-6354. 6. Smith TJ, et al. J Clin Endocrinol Metab. 2004;89:5076-5080. 7. Wang Y, et al. Ther Clin Risk Manag. 2019;15:1305-1318. 8. Patel A, et al. Am J Ophthalmol. 2019;208:281-288.

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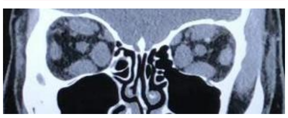
Compressive Optic Neuropathy (CON) Can Result in Irreversible Vision Loss

- Compressive Optic Neuropathy (CON) is a rare, serious complication of TED, affecting 4 to 8% of patients with TED[1-3]
- Caused by compression of optic nerve due to enlargement of rectus muscles and increased volume of periorbital tissue[3]
- May require urgent treatment with medical or surgical decompression to avoid permanent or progressive vision loss[3]

Compressive Optic Neuropathy in a patient with TED.



EOM, extraocular muscle; MRI, magnetic resonance imaging.

1. Bartley GB. *Trans Am Ophthalmol Soc.* 1994; 92:477-588. 2. Bartley GB, et al. *Am J Ophthalmol.* 1996; 121(3):284-290. 3. Neigel JM, et al. *Ophthalmology.* 1988; 95(11):1515-1521. 4. McKeag D, et al. *J Ophthalmol.* 2007; 91:455-458. 5. Fernandez E, et al. *Ann Thyroid Res.* 2016; 2:63-65

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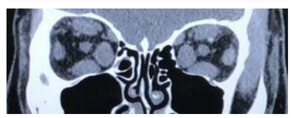
Clinical features of Compressive optic neuropathy

- Clinical features include[3,4]:
  - Slow, progressive loss of vision
  - Impairment of color vision
  - Optic disc swelling
  - Radiologic evidence of apical optic nerve compression
  - Relative afferent pupillary defect
  - Visual field defect
  - Optic atrophy (or edema)

Compressive Optic Neuropathy in a patient with TED.



EOM, extraocular muscle; MRI, magnetic resonance imaging

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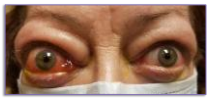
TED Has Broad Implications for Patients' Lives

Diminished Quality of Life

TED impacts the way patients see, the way they look, and the way they feel.[1-3]

In a study of 41 TED patients, **75.6% had altered visual function.**[2]



In a study of 41 TED patients, **95.1% perceived a disturbance in their appearance.**[2]

In another study with 102 TED patients, **45% had anxiety and/or depression.**[2]

1. Bothun ED et al. *Clin Ophthalmol.* 2009; 3:543-551. 2. Barrio-Barrio J et al. *J Ophthalmol.* 2015; 2015:249125. 3. Kahaly GJ et al. *Clin Endocrinol.* 2005; 63:395-402. 4. Delfino LC, et al. *Arch Endocrinol Metab.* 2017;61(4):374-381

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The Palpebral Fissure

- Normally 8-11 mm wide (vertically) and 27-30 mm long (horizontally)
- Large eye with shallow orbit = prominent globe with a wider fissure
- Forward displacement of globe= widening of palpebral fissure
- Abnormal recession of the globe into the orbit results in narrowing of the palpebral fissure

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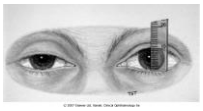
Exophthalmos

- Seen in Thyroid Disease
- Retraction of the upper eyelids causes a widening of the palpebral fissure
- Thyroid eye disease: Exophthalmometry measurements are remarkably similar to normal patients
- Vertical fissure measurements are better



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Measuring Protrusion

- the amount of protrusion of the normal eye can be important clinical marker
- protrusion is typically measured from the deepest part of the lateral orbital rim to the corneal apex
- Hertel exophthalmometer- most accurate
- Even a simple ruler can be used- screening

http://www.spkplenflestar.com/Products/examination_instruments/image/K-0161.jpg

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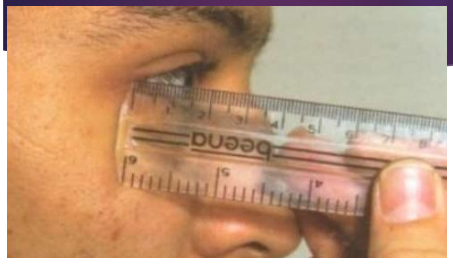

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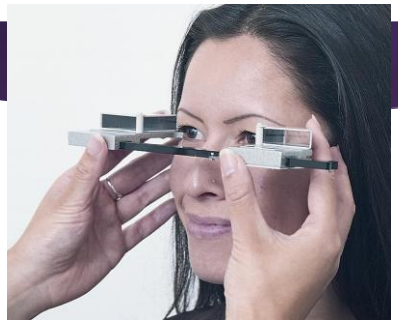

AAO.org Exophthalmometry

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Exophthalmometry measurement

- Measurements range from 12 to 21 mm -normal subjects
- mean of 16 mm
- thyroid eye disease yield values ranging from 12 to 24 mm
- mean of 18 mm.
- Measurements of greater than 19 mm however, were found in only about 5% of normals, while 32% of those with thyroid eye disease fell above this level.
- Lot of ethnic variations

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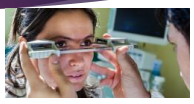
Proptosis Is Quantified With an Exophthalmometer



- Exophthalmometer is a noninvasive tool designed to measure the forward protrusion of the eye[1,2]
- Normal ocular protrusion as measured from the lateral orbital rim to corneal apex has traditionally been considered ≤21 mm in adults[2]
  - Protrusion >21mm or a 2-mm difference unilaterally or between the two eyes is considered abnormal
- However, proptosis upper limits of normal varies by age, sex, and race[2,3]

1. Bothun ED et al. *Clin Ophthalmol*. 2009; 3:543-551. 2. Barrio-Barrio J et al. *J Ophthalmol*. 2015; 2015:249125. 3. Kahaly GJ et al. *Clin Endocrinol*. 2005; 63:395-402. 4. Delfino LC, et al. *Arch Endocrinol Metab*. 2017; 61(4):374-381.

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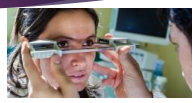
Upper limits of Proptosis

Race	Female	Male
African American	23 mm	24 mm
White	19 mm	21 mm
Asian	16 mm	17 mm (Thai) or 18.6 mm (Chinese)



1. Bothun ED et al. *Clin Ophthalmol*. 2009; 3:543-551. 2. Barrio-Barrio J et al. *J Ophthalmol*. 2015; 2015:249125. 3. Kahaly GJ et al. *Clin Endocrinol*. 2005; 63:395-402. 4. Delfino LC, et al. *Arch Endocrinol Metab*. 2017; 61(4):374-381.

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Gorman Bahn Diplopia Scale[4]

Diplopia Score
0. No diplopia
1. Intermittent, i.e., diplopia in the primary position of gaze, when tired or when first awakening
2. Inconstant, i.e., diplopia at extremes of gaze
3. Constant, i.e., continuous diplopia in primary or reading position

1. Bothun ED et al. *Clin Ophthalmol*. 2009; 3:543-551. 2. Barrio-Barrio J et al. *J Ophthalmol*. 2015; 2015:249125. 3. Kahaly GJ et al. *Clin Endocrinol*. 2005; 63:395-402. 4. Delfino LC, et al. *Arch Endocrinol Metab*. 2017; 61(4):374-381.

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Thyrotoxicosis

- Dalrymple's Sign

  Retraction of the upper lid(s)

- Von Grafe's Sign
  - Delay of movement of the upper lid when shifting gaze from up to down; causes a staring expression

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Clinical Activity Score Is a Measurement of TED Activity

For initial CAS, only score items 1-7	
1	Spontaneous orbital pain
2	Gaze-evoked orbital pain
3	Eyelid swelling that is considered to be due to active TED
4	Eyelid erythema
5	Conjunctival redness considered to be due to active TED
6	Chemosis
7	Inflammation of caruncle OR plica
Patients assessed after follow-up (1-3 months) can be scored out of 10 by including items 8-10	
8	Increase of ≥2 mm in proptosis
9	Decrease in uniocular excursion in any one direction of ≥5°
10	Decrease of acuity equivalent to ≥1 Snellen line

7-component scale commonly used to assess changes in disease activity in clinical trial settings.

- Clinical Activity Score (CAS) is based on four classical signs of inflammation: pain, redness, swelling and impaired function[1-3]
  - One point for each item, weight for each item is the same
  - Total CAS may range from 0 to 7 or 0 to 10
  - CAS ≥ 3 out of 7 on initial visit or CAS ≥ 4 out of 10 at follow-up visit implies active inflammatory stage of TED*
- Validated as a predictor of response to immunosuppression[1]
- ATA Guidelines and European Thyroid Association/EUGOGO recommend CAS to determine TED activity[2,3]

ATA, American Thyroid Association; EUGOGO, European Group of Graves' Orbitopathy.
*≥ 3 at initial visit and ≥ 4 at follow-up visit.
1. Mourits MP et al. *Br J Ophthalmol*. 1989; 73(8):639-644. 2. Ross DS et al. *Thyroid*. 2016; 26(10):1343-1421. 3. Bartalena L et al. *Eur Thyroid J*. 2016; 5(1):9-26. 4. Barrio-Barrio J et al. *J Ophthalmol*. 2015; 2015:249125.

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American Thyroid Association
TED Severity Grades

Mild TED[1]: Patients whose features of TED have only a minor impact on daily life, generally insufficient to justify immunosuppressive or surgical treatment.

Moderate-to-Severe TED: Patients without sight-threatening TED whose eye disease has sufficient impact on daily life to justify the risks of immunosuppression (if active) or surgical intervention (if inactive).

Sight-Threatening TED: Patients with optic neuropathy and/or corneal breakdown. This category warrants immediate intervention.

Grade[1]	Lid retraction	Soft tissues	Proptosis†	Diplopia	Corneal exposure	Optic nerve status
Mild	<2 mm	Mild involvement	<3 mm	Transient or absent	Absent	Normal
Moderate	≥2 mm	Moderate involvement	≥3 mm	Inconstant	Mild	Normal
Severe	≥2 mm	Severe involvement	≥3 mm	Constant	Mild	Normal
Sight threatening	—	—	—	—	Severe	Compression

The European Thyroid Association has similar severity grades with one exception. The severity grades of moderate and severe are combined to be Moderate/Severe. All of the signs and symptoms for ATA and ETA are the same[2]

†Proptosis refers to the protrusion compared to the upper limit of normal for each race/sex or the patient's baseline, if available.
1. Ross DS, et al. *Thyroid.* 2016; 26(10):1343-1421. 2. Bartalena L et al. *Eur Thyroid J.* 2016; 5(1):9-26.

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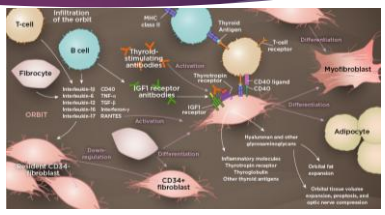
IGF-1R/TSHR Signaling Complex Activation Triggers Inflammatory Response Leading to Tissue Expansion and Remodeling

- Orbital fibroblasts (OFs) are the principal cells that drive the inflammation and expansion of orbital soft tissues[1-4]
- OFs from patients with TED are more prone to activation, leading to proliferation, differentiation into adipocytes and increased hyaluronan secretion than OFs from healthy controls[1,3,4]
- IGF-1R and TSHR are co-localized and form a signaling complex[5]



IGF-1R, insulin-like growth factor-1 receptor; TSHR, thyroid-stimulating hormone receptor.

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Historically, Treatment Options for TED Selected Based on Disease Activity and Severity[1,2]

Disease Severity

	Mild	Moderate-to-severe	Sight-threatening
Acute Stage	• Local measures* • Oral steroids if acute stage or decreased QoL	• IV steroids • Off-label biologics (TOCI, RTX) • Orbital radiation • Orbital decompression surgery or clinical trial enrollment	• IV steroids + urgent orbital decompression surgery
Chronic Disease	• Local measures	• Surgical intervention after ≥3 months observation (as needed)	• Surgical intervention

IV, intravenous; N/A, not applicable; QoL, quality of life; TOCI, tocilizumab; RTX, rituximab.
*With or without selenium supplementation.
1. Ross DS, et al. *Thyroid.* 2016; 26(10):1343-1421. 2. Bartalena L et al. *Eur Thyroid J.* 2016; 5(1):9-26.

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Teprotumumab-trbw Overview

FDA Indication
- **Teprotumumab is indicated for the treatment of Thyroid Eye Disease**
- Approved January 21, 2020[1]

Mechanism of Action
- Teprotumumab-trbw is a fully human monoclonal antibody[1] that binds to IGF-1R and blocks its activation and signaling

Administration
- One infusion every 3 weeks across 21 weeks (8 total infusions)[1]
- First infusion of 10 mg/kg followed by 7 infusions of 20 mg/kg[1]

IGF-1R, insulin-like growth factor-1 receptor;
1. Horizon Pharma USA, Inc. Treatment of Graves' orbitopathy (thyroid eye disease) to reduce proptosis with teprotumumab-trbw infusions in a randomized, placebo-controlled, clinical study (OPTIC). https://clinicaltrials.gov/ct2/show/NCT03298451. Accessed November 13, 2018.

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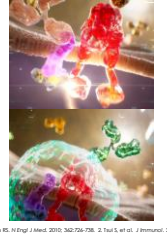
Mechanism of Action of Teprotumumab-trbw for TED



Pathophysiology of TED
- The body attacks its own orbital cells which overexpress IGF-1R.[1,2]
- IGF-1R and TSHR are co-localized and form a signaling complex.[2]
- This leads to severe inflammation and expansion of tissue, muscle and fat cells behind the eye.[1,3]
- May cause proptosis (bulging of the eyes) and optic nerve compression.[1,3]

Teprotumumab-trbw Mechanism of Action[3]
- Fully human monoclonal antibody inhibitor of IGF-1R.
- Blocks IGF-1R and turns off signaling complex at the source of the disease.
- Intended to reduce inflammation and prevent excessive cell growth behind the eye.

1. Bahn RS. *N Engl J Med.* 2010; 362:726-738. 2. Tsui S, et al. *J Immunol.* 2008; 181:4397-4405. 3. Smith TJ, et al. *N Engl J Med.* 2014; 373:1552-1565.

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OPTIC Study

Patient Criteria
- Active TED
- 18-80 years
- CAS ≥4
- <9 months since active TED onset with no prior treatment
- FT4 and FT3 <50% above or below normal limits

Week 0 — Week 24

Screening — Randomization

- Teprotumumab: 8 infusions (Q3W)
- Placebo: 8 infusions (Q3W)

Primary endpoint at Week 24
Percentage of participants with ≥2mm reduction in proptosis

Off-Treatment Follow-up Period

Douglas RS, et al. *N Engl J Med.* 2020;382(4):341–352

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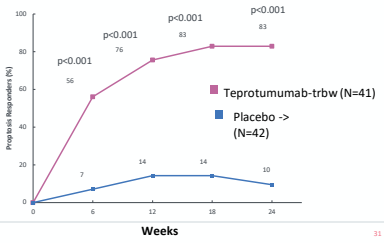
Proptosis Responders (≥ 2 mm reduction)



Douglas RS, et al. *N Engl J Med.* 2020;382(4):341–352.

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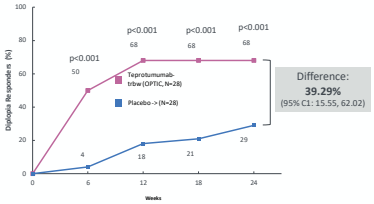
Diplopia Responders (≥ 1 grade improvement)



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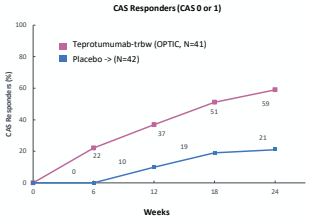
CAS score responders



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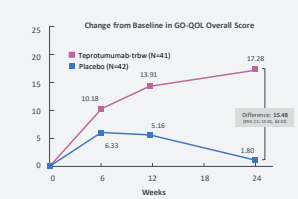
GO-QoL Improvements Overall



Drivers of decreased QoL:

- TED activity[1-4] and ocular pain[1,5]
- Disease severity[2-4,6,7]:
  - Proptosis[4,8-10] and asymmetric proptosis (≥2 mm difference between eyes)[4]
  - Diplopia[1,3-5,11]
  - Blurred vision[1]

MMRM ANCOVA model with an unstructured covariance matrix, including the following terms: baseline score, tobacco use status (non-user, user), treatment group, visit, and visit-by-treatment and visit-by-baseline-score interactions; least square mean +/- standard error.

1. Kahaly GJ, et al. *Clin Endocrinol (Oxf).* 2005; 63:395-402. 2. Choi YJ, et al. *Eye (Lond).* 2012; 26:546-551. 3. Lin IC, et al. *J Formos Med Assoc.* 2015; 114:1047-1054. 4. Villagelin D, et al. *Front Endocrinol (Lausanne).* 2016; 10:192. 5. Kahaly GJ, et al. *Thyroid.* 2002; 12:237-249. 6. Pana E, et al. *Br J Ophthalmol.* 2004; 88:75-78. 7. Dolfino JC, et al. *Arch Endocrinol Metab.* 2017; 61:376-381. 8. Bartalena L, et al. *Endocr Rev.* 2000; 21:168-199. 9. Gerding MN, et al. *Thyroid.* 1997; 7:881-889. 10. Tehrani M, et al. *Eur J Ophthalmol.* 2004; 14:193-198. 11. Bradley EA, et al. *Ophthalmology.* 2006; 113:1655-1664.

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Warnings, Precautions, and Special Populations

Infusion Reactions

- Teprotumumab-trbw may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with teprotumumab-trbw

Exacerbation of Preexisting Inflammatory Bowel Disease

- Teprotumumab-trbw may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of teprotumumab-trbw

Hyperglycemia

- Hyperglycemia or increased blood glucose may occur in patients treated with teprotumumab-trbw. In clinical trials, 10% of patients (two thirds of whom had pre-existing diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be controlled with medications for glycemic control, if necessary
- Assess patients for elevated blood glucose and symptoms of hyperglycemia prior to infusion and continue to monitor while on treatment with teprotumumab-trbw. Ensure patients with hyperglycemia or pre-existing diabetes are under appropriate glycemic control before and while receiving teprotumumab-trbw

Special Population

- Teprotumumab-trbw should not be used in pregnancy, and appropriate forms of contraception should be implemented prior to initiation, during treatment, and for 6 months following the last dose of teprotumumab-trbw

TEPEZZA. [teprotumumab-trbw] [prescribing information] Horizon.

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Adverse Reactions

Adverse Reactions Occurring in ≥5% of Patients Treated With Teprotumumab and Greater Incidence Than Placebo

Adverse Reactions	Teprotumumab (n=84), n (%)	Placebo (n=86), n (%)
Muscle spasms	21 (25%)	6 (7%)
Nausea	14 (17%)	8 (9%)
Alopecia	11 (13%)	7 (8%)
Diarrhea	10 (12%)	7 (8%)
Fatigue	10 (12%)	6 (7%)
Hyperglycemia	8 (10%)	1 (1%)
Hearing impairment	8 (10%)	0
Dysgeusia	7 (8%)	0
Headache	7 (8%)	6 (7%)
Dry skin	7 (8%)	0
Weight decreased	5 (6%)	0
Nail disorder	4 (5%)	0

Menstrual disorders like amenorrhea, metrorrhagia, and dysmenorrhea were reported in approximately 23% (5 of 22 patients) of menstruating women treated with teprotumumab-trbw compared to 4% (1 of 25 patients) treated with placebo in clinical trials.

1. TEPEZZA. [teprotumumab-trbw] [prescribing information]. Horizon.

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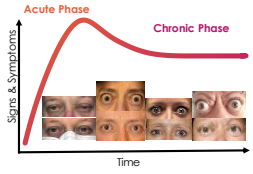
Evolving TED disease state understanding



"This treatment has the potential to alter the course of the disease, potentially sparing patients from needing multiple invasive surgeries by providing an alternative, nonsurgical treatment option."

- Wiley Chambers, M.D.,
Deputy Director of the Division of Transplant and Ophthalmology Products in the FDA's Center for Drug Evaluation and Research

Source: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-thyroid-eye-disease

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Efficacy and Safety of Teprotumumab in Patients With Thyroid Eye Disease of Long Duration and Low Disease Activity

Raymond S. Douglas,[1] Steven Couch,[2] Sara T. Wester,[3] Brian T. Fowler,[4] Catherine Y. Liu,[5] Prem S. Subramanian,[6,7] Rosa Tang,[8] Quang T. Nguyen,[9] Robi N. Maamari,[2] Shoaib Ugradar,[1] Kate Hsu,[10] Michael Karon,[10] and Marius N. Stan[11]

Context: Early inflammatory thyroid eye disease (TED) can lead to symptomatic chronic disease, including disabling proptosis. Teprotumumab, an insulin-like growth factor-1 receptor (IGF-1R) inhibitor, previously demonstrated efficacy in acute, high-inflammation TED trials.

Objective: We present data from the first placebo-controlled trial with teprotumumab in chronic/low disease activity TED.

42 Tx vs 20 Placebo
-2.41 vs 0.92 Proptosis
AE similar between groups

Conclusion: Teprotumumab significantly improved proptosis vs placebo in longstanding/low inflammation TED, demonstrating efficacy regardless of disease duration/activity. The safety profile was comparable to that previously reported.

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Thank You!

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