



THYROID EYE DISEASE

Also referred to as Graves' orbitopathy, Graves' ophthalmopathy, Graves' eye disease, thyroid-associated orbitopathy, or thyroid-associated ophthalmopathy



Thyroid Eye Disease (TED)

It is an autoimmune condition in which the immune system mistakenly attacks the muscles and fatty tissues behind the eyes. Although it is most commonly linked to Graves' disease, patients can develop TED even if thyroid levels are currently normal or even period



TED AND GRAVES' DISEASE

Graves' disease is an autoimmune condition that attacks the thyroid gland, causing the gland to secrete excess thyroid hormone

1

40-50% of patients with Graves' disease have signs and symptoms of TED

2

30% have moderate-severe disease

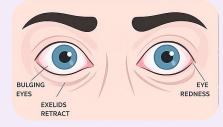
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5% have sight-threatening disease

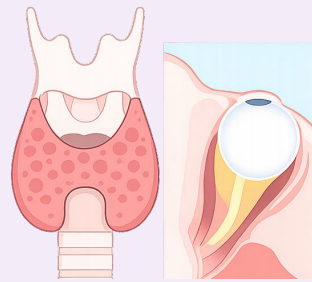
GRAVES' DISEASE



Normal EYE

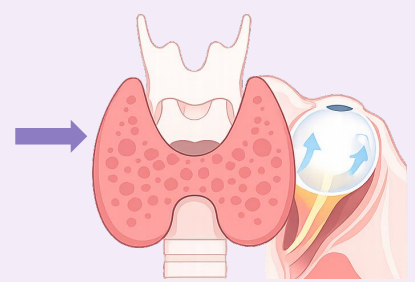


BULGING EYES



NORMAL THYROID GLAND

NORMAL EYE



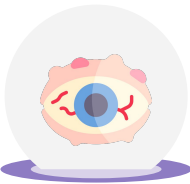
ENLARGED THYROID GLAND

EXOPHTHALMOS

Clinical Features of TED



Diplopia (Double vision)



Eye pain



Red watery eyes



Proptosis (Bulging eyes)



Light sensitivity



Gritty, dry eyes

Prevalence & Incidence

- Approximately 25 to 50% of Graves' disease cases present with thyroid eye disease
The estimated global prevalence is 0.1–0.3%—rare globally but common among patients with Graves' disease
- Associated with:
 - 90% Graves hyperthyroidism
 - 6% Euthyroidism
 - 3% Hashimoto thyroiditis
 - 1% Primary hypothyroidism



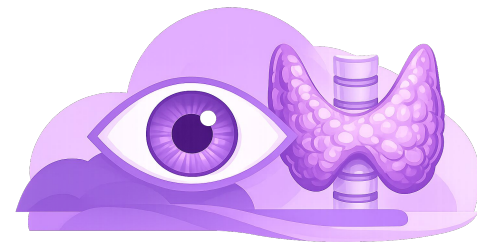
FEMALE-TO-MALE RATIO

The disease is more common in women than in men, although the female-to-male ratio is 1:4 in severe forms of eye disease



PREVALENCE

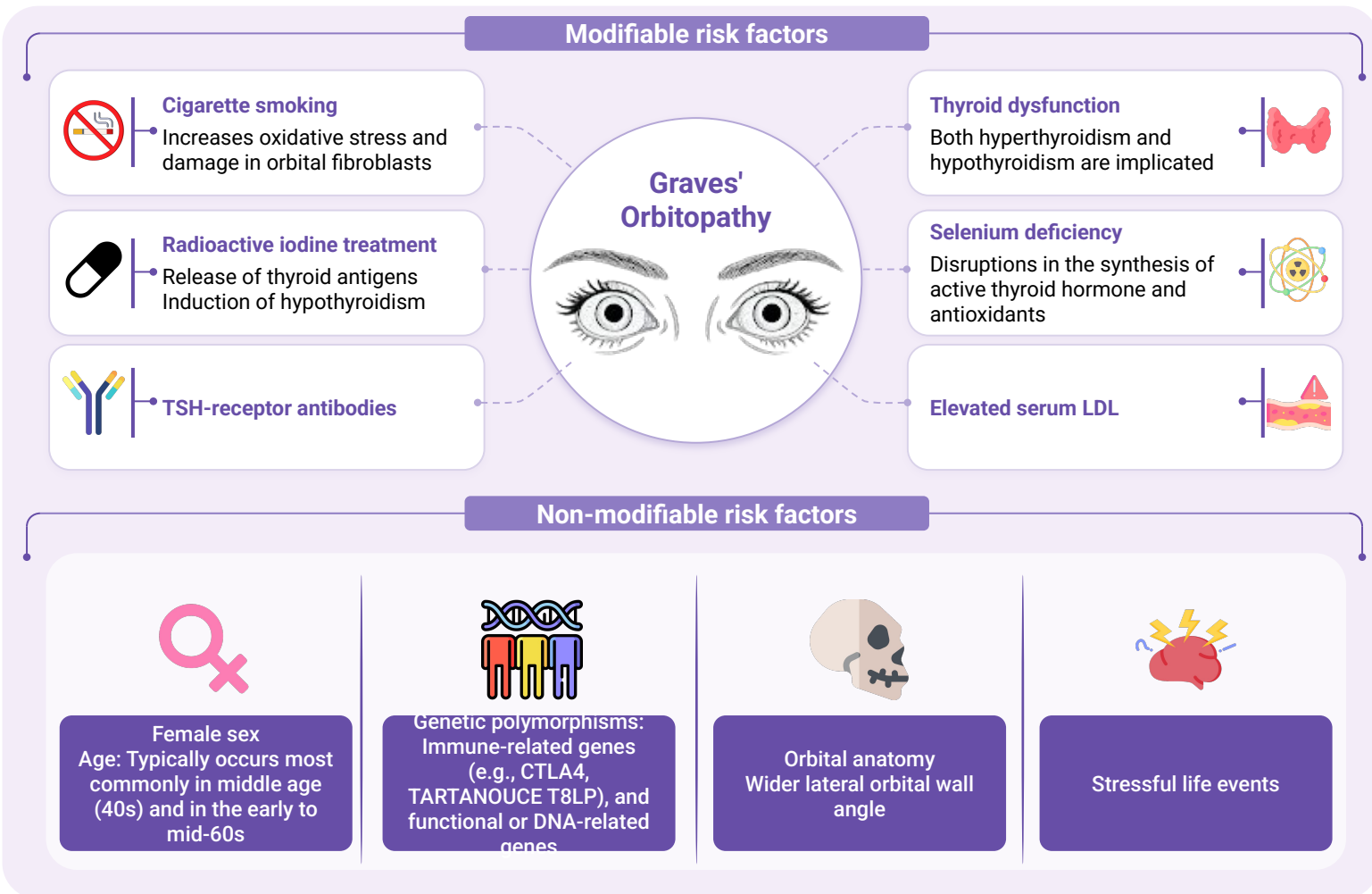
While TED affects fewer than 50% of Graves' patients, its overall prevalence in the general population is approximately 0.25%



YOUR EYES ARE SENSITIVE!

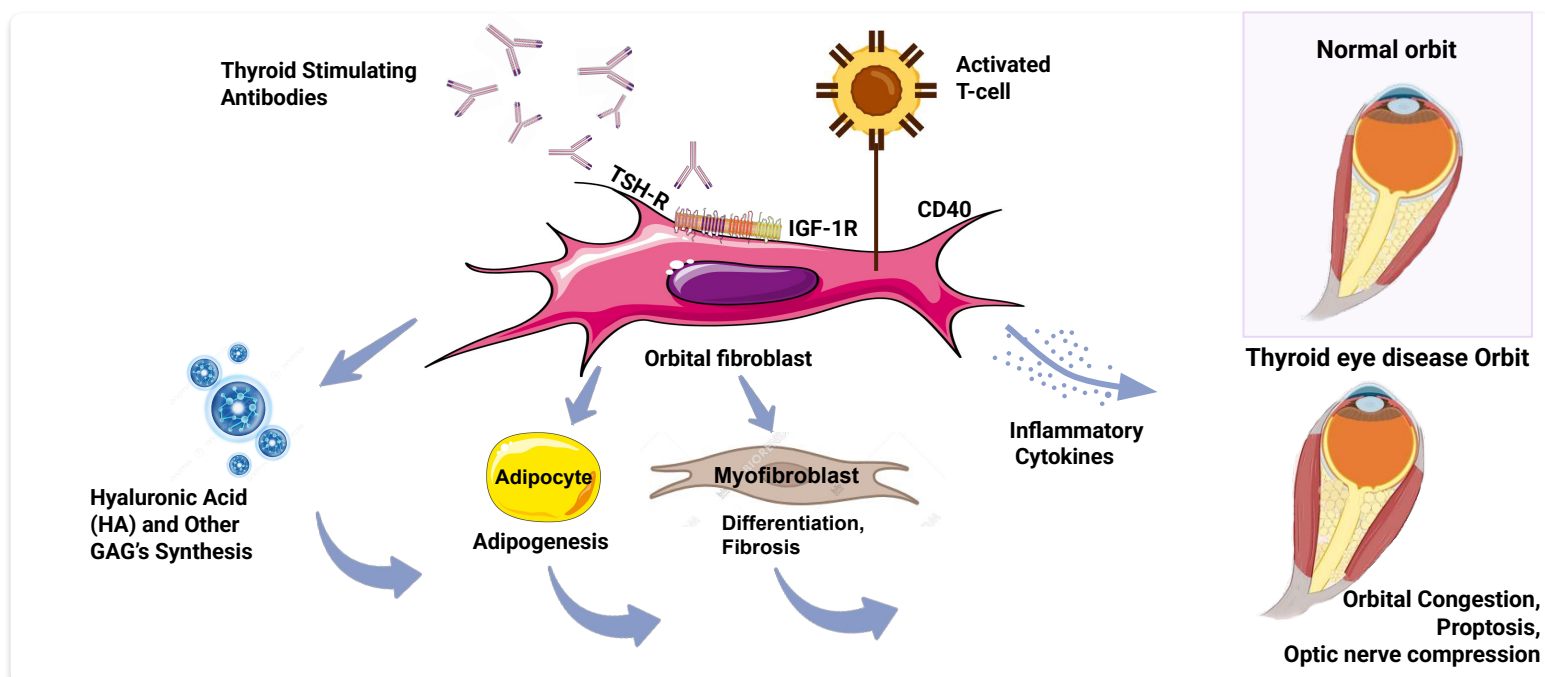
Receptors such as the thyroid-stimulating hormone receptor and the insulin-like growth factor 1 receptor are located around the eye and are recognized as foreign by the body. The body produces antibodies that attack these receptors, leading to swelling of the tissues around the eye

Key Risk Factors in Thyroid Eye Disease



Pathophysiology

TED in a case of "mistaken identity," in which the immune system attacks the tissues behind the eyes instead of the thyroid gland. Because the eye socket (the orbit) is a fixed "bony box," any swelling or growth inside has nowhere to go but forward



Phases Of TED

Thyroid Eye Disease (TED) progresses through two main phases:

1. Active Phase (Inflammatory Phase)



Ongoing inflammation and immune activity usually last 6 months to 2 years; symptoms are progressive and can worsen over time

Key features:

- Redness and swelling of eyes and eyelids
- Pain or pressure behind the eyes, light sensitivity
- Bulging eyes (proptosis), double vision (diplopia)

Most responsive to medical treatment during this phase

Active Phase



2. Inactive Phase (Fibrotic/Chronic Phase)



Begins when inflammation subsides

Disease becomes stable (non-progressive)

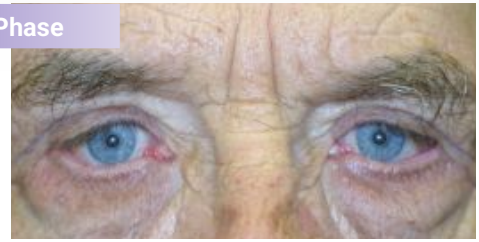
Key features:

- Permanent changes (e.g., eye bulging, lid retraction)
- Fibrosis (scarring) of tissues, double vision

Less responsive to drugs

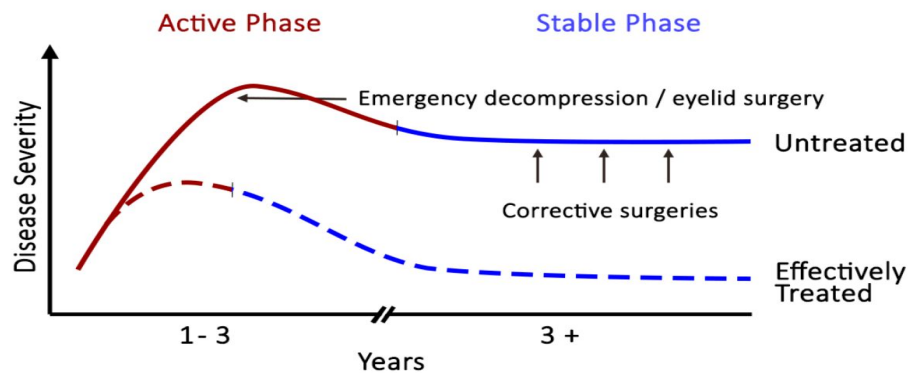
Surgical treatments (if needed) are usually done in this phase

Stable Phase



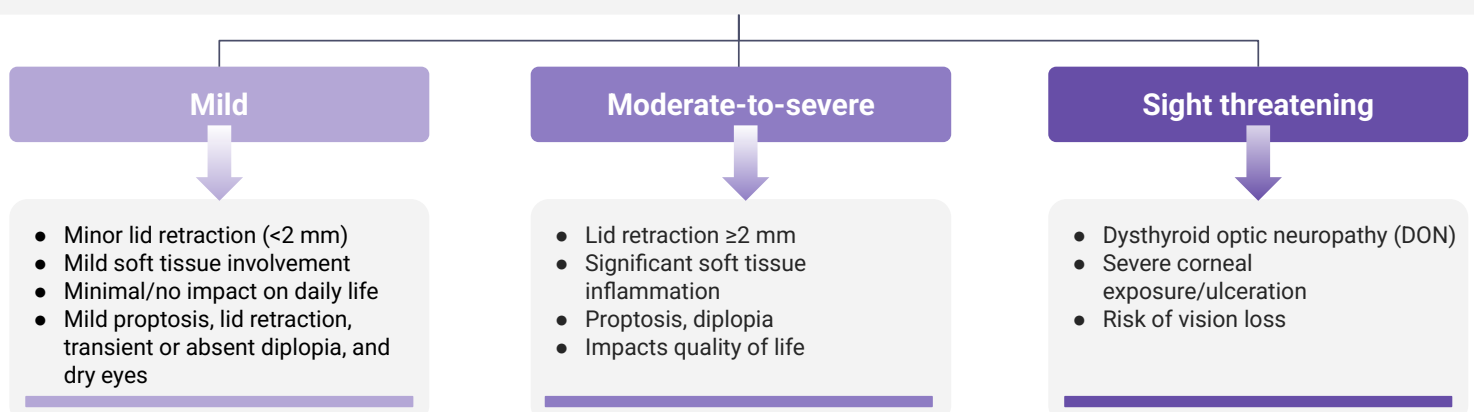
Rundle's Curve

TED typically follows Rundle's Curve, which consists of two main stages:



Severity Classification (EUGOGO)

According to the European Group on Graves' Orbitopathy (EUGOGO) classification system, TED is classified by



Diagnosis

TED severity is measured by the Clinical Activity Score (CAS), according to European Thyroid Association (ETA) guidelines. A CAS ≥ 3 usually indicates active inflammation



01

Blood test



02

CT or MRI Scan



03

Vision testing

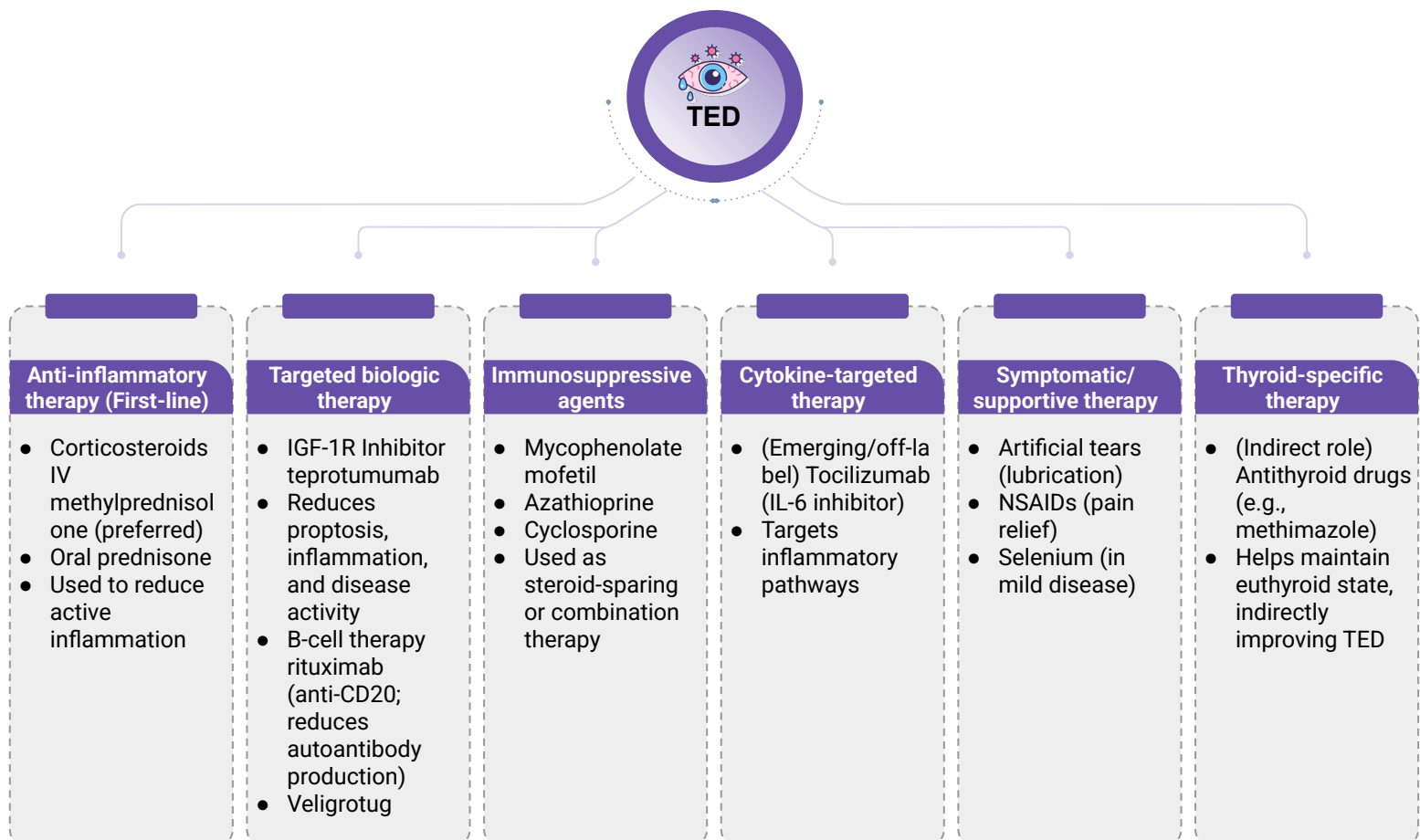


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Hertel Exophthalmometry

Current Treatments and Emerging Pipeline in TED

Classification of Therapeutic Interventions in Thyroid Eye Disease (TED)



Approved Therapies and Clinical Trial Benchmarks for TED



Approved Drug

Currently, teprotumumab (Tepezza, Amgen) is the only FDA-approved drug for the treatment of thyroid eye disease

Thyroid Eye Disease (TED) - Approved Drugs

Company	Approval Date	Geography	Brand	INN	MoA	RoA	Modality
	21-Jan-20	US		Teprotumumab	Anti-IGF-1R mAb	IV	Monoclonal Antibody
	24-Sep-24	Japan					
	19 June 2025 7-May-25	EU UK					

Innovent

In March 2025, Innovent Biologics received approval from China's National Medical Products Administration (NMPA) for SYCUME (**teprotumumab N01**), a recombinant anti-IGF-1R monoclonal antibody, for the treatment of thyroid eye disease (TED)



Clinical Trial Endpoints in Thyroid Eye Disease

The primary gold standard for FDA approval is the proptosis responder rate, as reduction in eye bulging was historically the hardest symptom to treat without surgery

Primary Efficacy Endpoints

Proptosis Reduction

A decrease in the protrusion of the study eye by ≥ 2 mm from baseline, without a corresponding increase in the other eye

Clinical Activity Score (CAS) Reduction

A decrease in CAS by ≥ 2 points, indicating a significant drop in active inflammation (redness, swelling, and pain)

Overall Responder Rate

The percentage of patients who achieve both the ≥ 2 mm proptosis reduction and the ≥ 2 point CAS reduction.

Secondary Efficacy Endpoints

Diplopia (Double Vision) Resolution

Measured by the percentage of patients whose double vision disappears or significantly improves (e.g., moving from constant to intermittent)

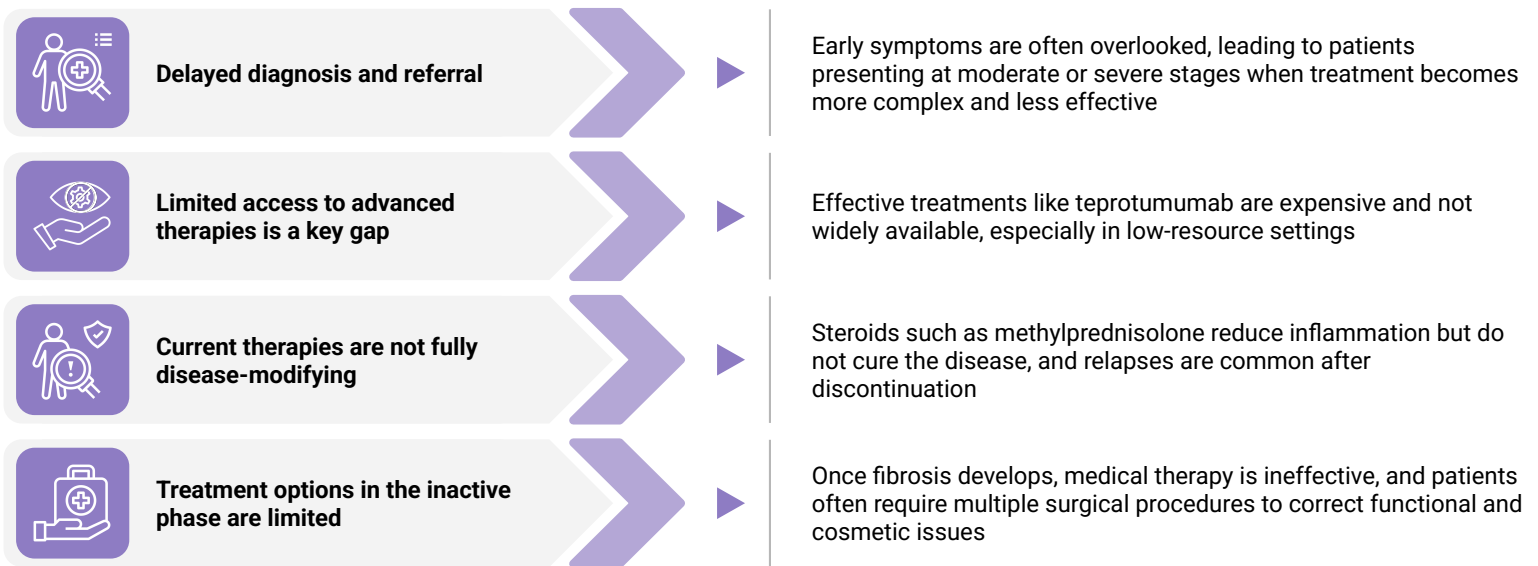
CAS

The percentage of patients who reach a state of "minimal to no" clinical inflammation

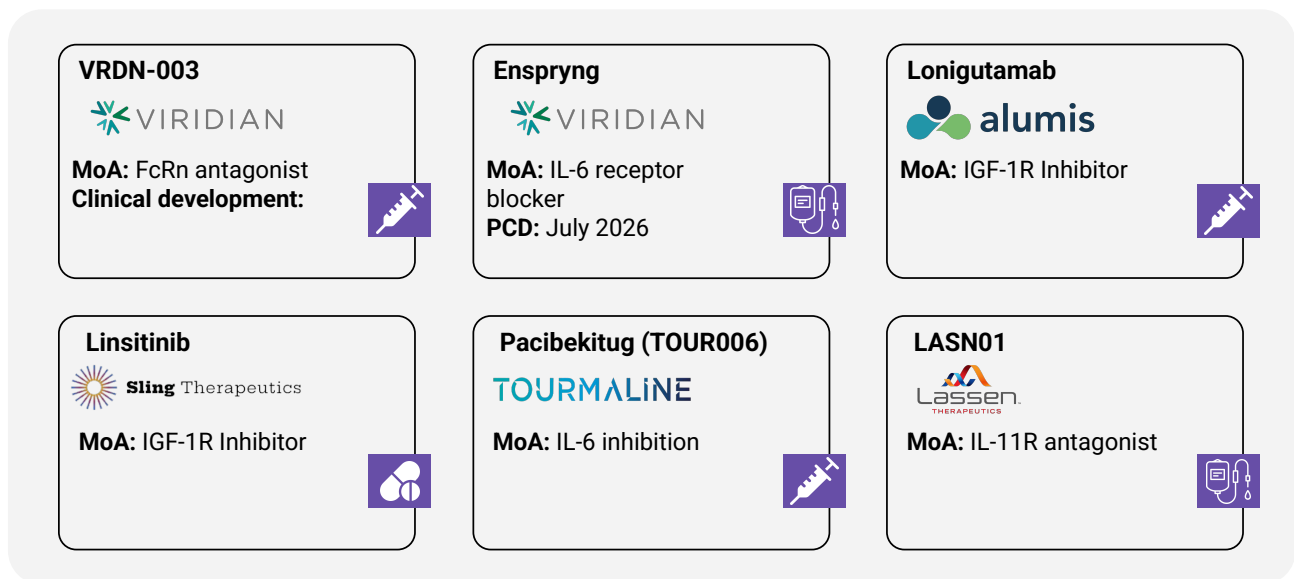
Quality of Life

Patients complete a 16-item questionnaire assessing how TED affects their daily life, including visual function (driving, reading) and appearance (self-confidence)

Treatment Gaps in Thyroid Eye Disease



EMERGING DRUGS



Conclusion

Importance of Early Intervention



The "active phase" (typically the first 6–36 months) represents a critical window for medical treatment. Using tools like the Clinical Activity Score (CAS) allows clinicians to use biologics or steroids when they are most effective at preventing permanent tissue expansion and scarring

Shift Toward Targeted Biologics



The treatment paradigm has shifted from broad immunosuppression (steroids) to targeted therapies such as IGF-1R inhibitors. These modern treatments have set new benchmarks in clinical trials by successfully reducing proptosis (bulging) and diplopia without the need for initial surgery

Need for Comprehensive Management



Successful outcomes depend on a "total care" approach: Strict smoking cessation, maintaining stable thyroid function (euthyroidism), and managing both the active inflammatory and the stable fibrotic stages



Early diagnosis and multidisciplinary care can help **protect vision** and **improve quality of life**