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Graves' Ophthalmopathy/ Thyroid Eye Disease

An underestimated disease with more than a billion-dollar opportunity!

Why are we talking about it

~50% of GD patients have clinically relevant graves ophthalmopathy

Can worsen despite good thyroid control

Can cause blindness or severe double vision

*Disfigurement and impact on QoL
Usually worse than clinical severity*



Poor clinical outcome

No effective medical cure

*High rate of misdiagnoses and lack of specialists
who can treat patients with GO*

*No animal model, how is the immune tolerance
broken*

TED is an autoimmune condition characterized by inflammation, growth, and damage to tissues around and behind the eyes

Autoantibodies trigger **IGF-1R**/TSHR pathway

Heterogeneous **autoimmune disease** with clinical signs and symptoms that can vary or modulate following onset, in some cases for **the rest of a patient's life**

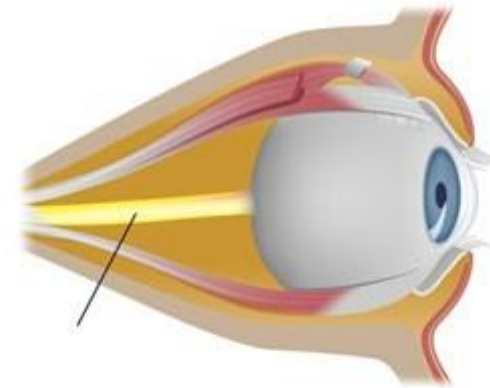
Main signs include **proptosis** (eye bulging), redness, swelling, **diplopia** (double vision), and lid retraction

Severe cases can cause **sight-threatening optic nerve compression**

An estimated **190K people in the US** alone have moderate to severe TED

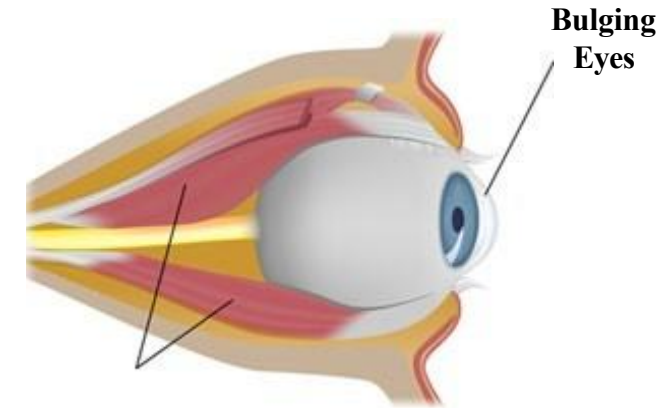
GO remains largely **undiagnosed** due to **less awareness** among the treating physicians and asymptomatic nature of the disease

Normal Eye Anatomy



Optic Nerve

Thyroid Eye Disease (TED)



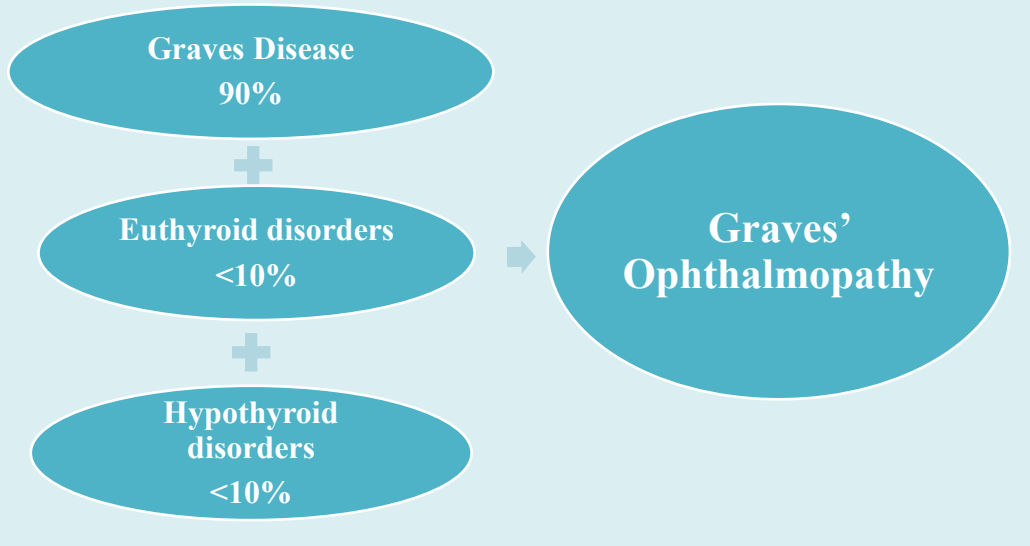
Enlargement of extraocular muscles

People living with TED experience proptosis, redness, swelling, diplopia, and lid retraction



A not so rare, chronic, heterogeneous debilitating autoimmune disorder of the eyes

Majority of GO cases are caused due to Graves Disease, and only a small percentage of these patients arise from other euthyroid or hypothyroid disorders.



As per the Estimates, as of 2024, ~2.4 million people were living with Graves' Ophthalmopathy across 7 MM

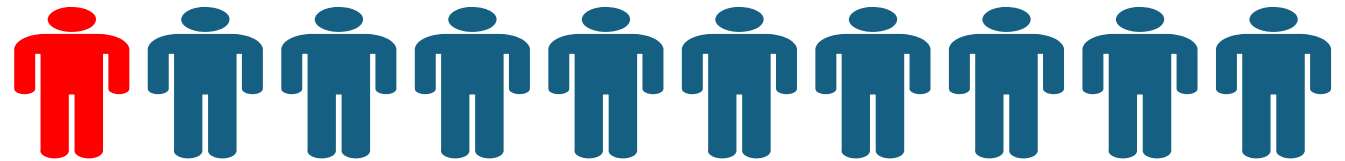
Growth Factors

- Smoking
- Aging population
- Family History for Autoimmune diseases
- Hypercholesterolemia



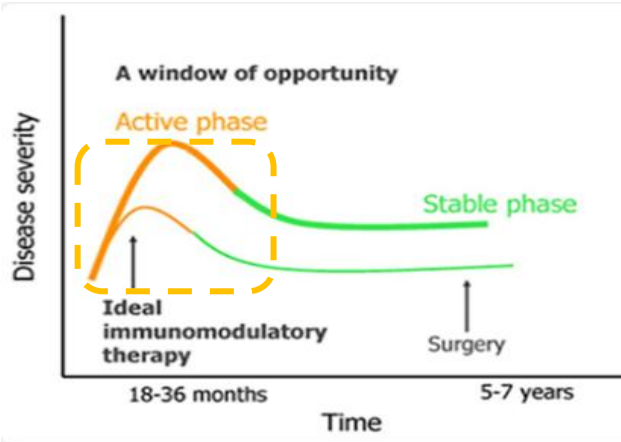
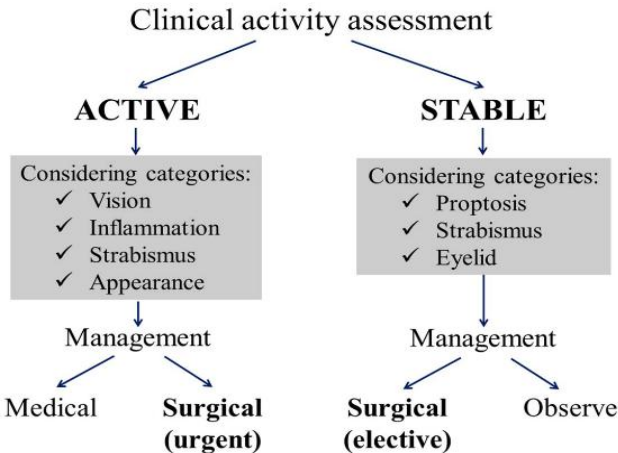
Females constitute ~80% of the prevalent population.

tends to be more severe in men, in whom it occurs at an older age than in women



3–5% may develop sight-threatening disease, such as Compressive optic neuropathy or exposure keratopathy

Current pharmacological management options target only 1/10th of the diagnosed population



TEPEZZA : one of the most successful rare disease medicine launches in history

First ever drug to be approved by the US FDA for the management of Graves’ Ophthalmopathy

Only pharmaceutical option to have proven efficacy in treating chronic GO patients

Established itself as the SOC: Tepezza has become a go-to treatment for moderate to severe TED, unseating orbital decompression as the most used treatment

The efficacy seen in clinical studies has well translated into real world making TEPEZZA the Only drug therapy which has shown clinical improvement in the proptosis

CURRENT THERAPIES

Active/ Acute Phase (Inflammatory phase) ~30% patients are in active phase at a given point of time	Mild	Tear supplement, Selenium
	Moderate to Severe	Steroids, Immunosuppressants, radiotherapy, Tepezza, Other biologics
	Sight Threatening	Surgical intervention
Stable/ Chronic Phase (Fibrotic Phase)	Surgical Intervention is the only available option TEPEZZA has been approved very recently in April 2023	



“Successful treatments (TEPEZZA) typically lead to new competitors but I do not see any threats to TEPAZZA for at least five years looking at the current pipeline therapies” KOL, FRANCE

TED arena is finally beginning to evolve...New drugs with the potential to provide sustained benefits are expected to contribute to the exponential market growth

Key competitors in Pipeline

Drug name	Developer	Phase	Patient segment	MoA	RoA	Expected launch year	Analyst Comments
Batoclimab	Immunovant Sciences	III	Moderate-to-severe active GO	Neonatal Fc receptor antagonists	SC	US- 2025	Convenient route of administration
Veligrotug (VRDN-001)	Viridian Therapeutics	III	Moderate-to-severe active GO	Insulin-like growth factor-I receptor antagonists	IV	US- 2025 EU & JP- 2026	- Direct competitor to TEPEZZA - Superior efficacy seen in clinical trials - BLA planned 2H 2025; EU MAA submission 1H 2026
VRDN-003	Viridian Therapeutics	III	Moderate-to-severe active GO	Insulin-like growth factor-I receptor antagonists	SC	US- 2025 EU & JP- 2026	- Topline data expected in 1H 2026 - BLA submission: Year-end 2026
Satralizumab	Chugai Pharmaceutical (Roche)	III	Moderate-to-severe active GO	Interleukin-6 receptor antagonist	SC	US- 2025 EU & JP- 2026	BLA submission: Year-end 2026

Unmet Needs

Limited treatment options

Teprotumumab is only approved in the U.S. for Graves' ophthalmopathy. Limited trials, availability, cost concerns, and uncertainties about surgery needs prevent approval in Europe and Japan. Additionally, its relapse rate (30%) is comparable to IV steroids (31%)

Disease burden

- GO requires long-term immunosuppressive and surgical treatment, leading to high direct and indirect costs.
- Direct costs come from therapy expenses, while indirect costs arise from work disability and sick leave.
- The disease significantly impacts QoL, causing psychosocial challenges.
- Women are primarily affected, further amplifying its social burden



Diagnostic challenge

- Early referral is crucial, but diagnostic barriers delay treatment.
- No specific tests, leading to misdiagnosis or delayed diagnosis.
- Symptoms overlap with other conditions, like allergies or conjunctivitis.
- Patients often mistakenly receive Graves' disease treatment instead of specialized care.
- Requires multiple specialist consultations for confirmation

Access barriers

- TEPEZZA is FDA-approved for GO but has restricted access due to insurance coverage limitations.
- Primarily used for acute moderate-to-severe cases, with limited usage in chronic or mild cases.
- High cost and lack of large-scale trials contribute to limited accessibility.
- Expanded trials and cost reduction could help make it a standard first-line therapy globally.

SWOT ANALYSIS



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STRENGTHS

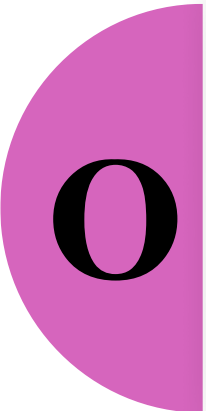
- The FDA approval of TEPEZZA has accelerated research and development in GO
- Awareness campaigns aim to improve early diagnosis and treatment of GO
- A collaboration between the American Thyroid Association and the European Thyroid Association resulted in a clinical guide providing multidisciplinary care recommendations based on the latest evidence from international experts.



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WEAKNESSES

- Limited understanding of disease progression affects clarity on response durability and relapse rates
- Inflammation in GO can impact ocular muscles, leading to diplopia and difficulty with daily activities like reading and driving
- CT imaging, though preferred for orbital decompression planning, has limitations in assessing orbitopathy activity, soft tissue edema, and exposes patients to radiation risks.



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OPPORTUNITIES

- Ocular drug discovery requires designing molecules with precise delivery to the target compartment that enhances efficacy, minimizes side effects, and improves treatment outcomes in eye diseases.
- No disease-modifying treatments exist for chronic patients, impacting their emotional and social well-being
- Advances in TED molecular research have led to targeted therapies like teprotumumab, which reduces progressive muscle and fat expansion.



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THREATS

- New therapeutics discovery and development for ocular diseases have been traditionally associated with a low probability of technical and regulatory success
- Being a rare disease, the inherent small patient population ends up being a critical challenge in drug development
- Although several monoclonal antibodies and anti-cytokine drugs are currently being developed for the treatment of GO, the high cost of such therapies often limits their use significantly in clinical practice

Research Methodology

Secondary Research

The secondary research on internal and external sources is being carried out to source qualitative and quantitative information relating to each market. The secondary research sources that are typically referred to include, but are not limited to:

- Company websites, annual reports, financial reports, broker reports, investor presentations, and SEC Filings
- Industry trade journals and other literature
- Internal and external proprietary databases
- National government documents, statistical databases, and market reports
- News articles, press releases, and webcasts specific to the companies operating in the market



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Thank you