THRIVE Phase 3 Trial of Veligrotug in Active Thyroid Eye Disease (TED): Efficacy, Safety, and Quality of Life at 15 Weeks

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KEY TAKEAWAYS

- **Veligrotug** led to robust and significant improvements in proptosis, diplopia, and disease activity at Week 15, with p<0.0001 for the primary and all secondary endpoints.
- These improvements translated to rapid and clinically meaningful improvements in QoL on the GO-QOL overall scale and both subscales; improvements were observed as early as 3 weeks and reached values well over the minimally important change (8 points) at Week 15.
- **Veligrotug** was generally well tolerated, with mostly mild AEs, and 96% of patients completing the treatment course.
- Results suggest **veligrotug** may become a promising new treatment option in TED.

INTRODUCTION

- TED is a debilitating disease significantly impacting visual function, QoL, and mental health. More treatment options are needed to improve convenience, efficacy and/or safety.
- **Veligrotug**, a full antagonist humanized mAb to IGF-1R, was assessed in THRIVE in active TED (onset within ≤15 months, proptosis ≥3 mm above normal, and CAS ≥3). Patients received either 10 mg/kg **veligrotug** or placebo given Q3W for a total of 5 IV infusions.
- Safety and efficacy including proptosis, diplopia, CAS, and GO-QOL were evaluated at Week 15.
  - CAS is a 7-point scale used to assess TED-related inflammatory activity
  - GO-QOL is a disease-specific questionnaire that assesses QoL in TED
- See RCOphth ePoster for THRIVE-2 results in chronic TED.

BASELINE CHARACTERISTICS

	Veligrotug (n=75)	Placebo (n=38)
Age, mean years (SD)	48.9 (12.4)	49.1 (12.5)
Female, % (n)	75% (56)	82% (31)
Proptosis (Hertel), mean mm (SD)	23.2 (3.1)	23.2 (3.3)
CAS, mean (SD)	4.5 (1.0)	4.8 (1.1)
Diplopia at baseline, % (n)	67% (50)	68% (26)
Diplopia, mean Gorman score (SD)[1]	2.0 (0.8)	2.0 (0.7)
Time since onset of TED signs/symptoms, mean months (SD)	7.9 (3.7)	7.2 (3.8)
GO-QOL, mean overall score (visual function + appearance)	53.3	59.1
GO-QOL, mean visual function subscale score	60.9	64.2
GO-QOL, mean appearance subscale score	45.9	54.2

[1]In patients with diplopia at baseline.

EFFICACY AND SAFETY AT WEEK 15

Efficacy endpoints		Veligrotug (n=75)	Placebo (n=38)	p-value
Overall Response	Overall responder rate (Hertel)[1]	67%	5%	p < 0.0001
Proptosis (Hertel)	Proptosis responder rate[2]	70%	5%	p < 0.0001
	Proptosis mean CFB, mm	-2.89	-0.48	p < 0.0001
Proptosis (MRI/CT)	Proptosis responder rate	69%	9%	p < 0.0001
	Proptosis mean CFB, mm	-2.91	-0.58	p < 0.0001
Diplopia	Diplopia complete resolution[3]	54%	12%	p < 0.0001
	Diplopia responder rate[4]	63%	20%	p < 0.0001
CAS	CAS 0 or 1	64%	18%	p < 0.0001
	CAS mean CFB	-3.4	-1.7	p < 0.0001

Endpoints shown are primary or secondary endpoints in at least one region. Missing values were imputed using prespecified imputation methodology. Results were obtained from a GEE model with an unstructured covariance matrix. [1]Primary endpoint in Europe and Australia: percentage of participants with ≥2-mm reduction in proptosis (by Hertel) AND ≥2-point improvement in CAS from baseline in the study eye, without corresponding deterioration (≥2-mm/point increase) in proptosis or CAS in the fellow eye. [2]Primary endpoint in North America: percentage of participants with ≥2-mm reduction in proptosis from baseline in the study eye (by Hertel), without deterioration in the fellow eye (≥2-mm increase). [3]Percentage of participants reporting baseline diplopia (Gorman score >0) and a score of 0 at Week 15. [4] Percentage of participants reporting a score reduction of at least 1 on the Gorman subjective diplopia scale, among patients with diplopia at baseline.

AEs occurring at ≥10% frequency in either arm Patients, % (n)	Veligrotug (n=75)	Placebo (n=38)
Muscle spasms	43% (32)	5% (2)
Headache	21% (16)	13% (5)
Infusion related reaction	17% (13)	3% (1)
Hearing impairment[1]	16% (12)	11% (4)
Hyperglycemia[1]	15% (11)	5% (2)
Fatigue[1]	13% (10)	16% (6)
Nausea	13% (10)	8% (3)
Ear discomfort	12% (9)	3% (1)
Diarrhea	11% (8)	3% (1)
Alopecia	8% (6)	11% (4)
Menstrual disorders[1,2]	24% (8/34)	8% (1/12)

Six unrelated serious AEs in 4 patients: cellulitis, appendicitis, dyspnea, hyperthyroidism, aortic dissection (planned surgery for known Type B aortic dissection), depression (diagnosed prior to 1st dose). [1]Includes multiple terms aggregated using standard sets of MedDRA terms. [2]Reported as percentage of menstruating women.

- Most AEs were mild in both arms: 74% vs 81% for **veligrotug** vs placebo.
- There was a low treatment discontinuation rate of 4% in the **veligrotug** arm.
- Serious AEs occurred in 4 **veligrotug** and no placebo patients; none were treatment-related.

GO-QOL OUTCOMES*

Overall

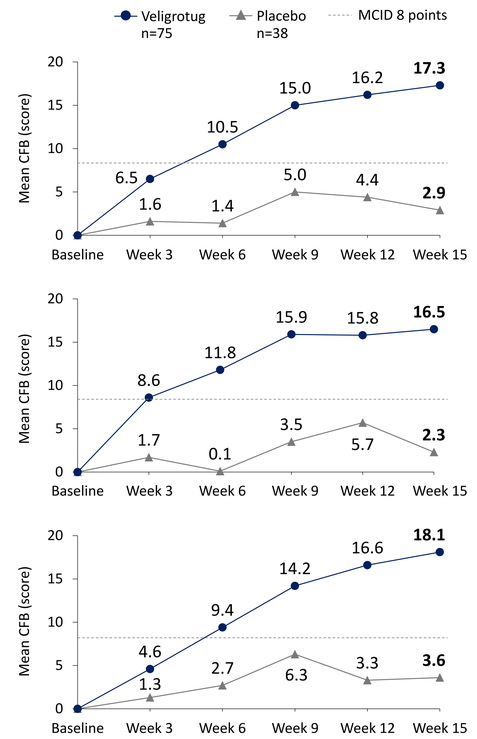
(comprised of 2 subscales, with 8 questions each [scale 0-100])

Visual function subscale

(limitations in activities: biking, walking, driving, reading, watching TV, moving around house, and hobbies)

Appearance subscale

(psychosocial influence: changed appearance, reactions from others, self-confidence, social activities, and relationships)



*Prespecified exploratory analysis at Week 15 and post hoc at earlier timepoints. GO-QOL MCID (minimal clinically important difference) vs baseline is 8 points. Nominal p <0.01 for all at Week 15.

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PDF of poster and additional information including THRIVE Study Group: Scan QR code.

Abbreviations used in poster: AE, adverse event; CAS, clinical activity score; CFB, change from baseline; GEE, generalized estimating equations; GO-QOL, Graves' Ophthalmopathy Quality of Life questionnaire; IGF-1R, insulin-like growth factor-1 receptor; IV, intravenous; mAb, monoclonal antibody; MedDRA, Medical Dictionary for Regulatory Activities; SD, standard deviation; QoL, quality of life; Q3W, every 3 weeks; TED, thyroid eye disease.

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