Durability of Treatment Response With VRDN-001, a Full Antagonist Antibody to IGF-1 Receptor, in Patients With Thyroid Eye Disease (TED): Phase 1/2 Clinical Study

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VRDN-001 is an investigational therapy not approved in any country.

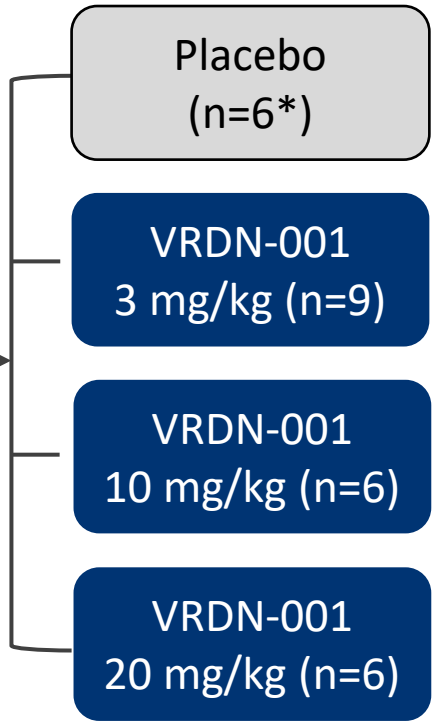
Poster#
FRI-545

ENDO2023

VRDN-001 POC randomized, double-masked trial tested 3 doses in active TED

2 infusions 3 weeks apart

Patients with active TED:
- CAS of ≥4
- Onset of signs/symptoms within prior 12 months



*2 patients were randomized to each placebo arm and 1 patient in the 3 mg/kg cohort's placebo arm discontinued the study before Week 6 and thus is not included in the efficacy analysis but is included in the safety analysis.
Clinical activity score (CAS) = a composite 0-7 scale scoring signs and symptoms of TED.

Baseline characteristics	Placebo (n=5)	All VRDN-001 (n=21)
Proptosis, mean (SEM)	22.8 (2)	23.7 (0.7)
CAS, mean (SEM)	5.0 (0.5)	5.4 (0.2)
Diplopia, n (%)	3 (60%)	13 (62%)
Diplopia, mean (SEM)	1.6 (0.7)	1.3 (0.3)
Months since onset, mean (SEM)	7.0 (2.0)	7.4 (0.8)
Age, mean years (SEM)	44.2 (4.3)	47 (3.3)
Female, n (%)	3 (60%)	19 (90%)

SEM = Standard error of the mean

Preliminary data: Efficacy measures at 6 weeks

	Overall responder rate	Proptosis responder rate	CAS: Score of 0 or 1	CAS: Mean change	Diplopia: Complete resolution*
All VRDN-001 (n=21)	67%	71%	62%	-4.1	54%
3 mg/kg, n=9	56%	67%	67%	-4.2	20%
10 mg/kg, n=6	83%	83%	83%	-4.3	75%
20 mg/kg, n=6	67%	67%	33%	-3.7	75%

*Diplopia was present at baseline in a subset of patients.

Preliminary durability of response at 12 weeks in VRDN-001 10 mg/kg cohort:

- Mean proptosis and CAS remained consistent
- 80% (4/5) of VRDN-001 responders at 6 weeks maintained proptosis response, overall response, and CAS decrease to 0 or 1
- Diplopia resolution achieved/maintained for all 4 patients who presented with diplopia at baseline

Safety profile

Data cutoff December 19, 2022

No SAEs, infusion reactions, or discontinuations

Adverse Reactions	Placebo (n=6)	VRDN-001 3 mg/kg (n=9)	VRDN-001 10 mg/kg (n=6)	VRDN-001 20 mg/kg (n=6)
Muscle spasms	-	2	2	2**
Nausea	-	2	-	-
Alopecia	1	-	-	-
Diarrhea	-	1	2**	1*
Fatigue	3	-	1	-
Hyperglycemia	-	1	-	1*
Hearing impairment	-	1	1	-
Dysgeusia	-	-	-	1
Headache	2**	2	1	1
Dry skin	-	1	-	1
Infusion reactions	-	-	-	-

*Deemed unrelated to study drug by the masked investigators.
** 1 patient deemed related and 1 patient deemed unrelated to study drug by the masked investigators.

Data are as of data cut-off of December 19, 2022. Other AE that occurred in more than 1 patient and deemed related to study drug by masked investigators was acne (n=2). Instances were mild and did not require intervention. Muscle spasms were mild and did not require intervention; hearing impairment (n=2) resolved without intervention in both cases. Both patients with hyperglycemia were diabetic at baseline; in 1 case glucose variability was determined by masked PI to be unrelated to drug.

2 days before
1st dose of VRDN-001

Week 0

- Proptosis: 29 mm
- CAS: 7

2 days after
2nd dose of VRDN-001

Week 6

- Change in proptosis by exophthalmometry: -5 mm
- Change in proptosis by MRI: -5.2 mm
- Change in CAS: -6 points

Case report patient information and photos taken by patient used with patient and investigator permission. Measures shown at baseline and Week 6 are for the study eye. Patient received 2 infusions in the study; in extended follow-up off treatment, TED symptoms have returned for this patient.

Conclusions

- Based on the preliminary results of this phase 2 POC study, further investigation is warranted of VRDN-001 for the potential treatment of TED.
- The efficacy and safety of VRDN-001 for the treatment of patients with active TED will be further assessed in the ongoing THRIVE phase 3 clinical trial (NCT05176639).