A multiple ascending dose (MAD) safety, tolerability and efficacy study of VRDN-001, a humanized monoclonal antibody directed against the IGF-1 receptor, in normal healthy volunteers (NHVs) and subjects with thyroid eye disease (TED)

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This study has been transitioned to CTIS with ID 2024-512244-36-00 check the CTIS register for the current data. The objectives of this are to establish the safety, tolerability, and efficacy of VRDN-001, and the pharmacokinetic (PK) and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51573

Source
ToetsingOnline

Brief title
VRDN-001-1001

Condition

- Other condition
- Eye disorders NEC

Synonym

Graves' disease, thyroid eye disease

Health condition

Thyroid Eye Disease (MedRA V23.1, system organ class. 100000004853, classification code: 10084358)

Research involving
Human

Sponsors and support

Primary sponsor: Viridian Therapeutics, Inc.
Source(s) of monetary or material Support: Industry

Intervention

Keyword: multiple ascending dose (MAD), safety, thyroid eye disease (TED), VRDN-001

Outcome measures

Primary outcome

Primary Efficacy Endpoint in the USA, Canada and China in the Pivotal portion

of the Study (THRIVE):

• Proptosis Responder Rate in the study eye (i.e., reduction of proptosis of >=

2 mm from baseline [without a corresponding increase of >= 2 mm in the fellow

eye] as measured by exophthalmometer) at 3 weeks post the fifth infusion (i.e.,

Week 15)

Primary Efficacy Endpoint in Australia, EU and UK in the Pivotal portion of the

Study (THRIVE):

• Overall Responder Rate comprised of Proptosis Responder Rate in the study eye

(i.e., reduction of proptosis of >= 2 mm from baseline [without a corresponding

increase of >= 2 mm in the fellow eye] as measured by exophthalmometer) at 3

weeks post the fifth infusion (i.e., Week 15) and Clinical Activity Responder

Rate in the study eye (i.e., reduction in CAS >= 2 points from baseline [without a corresponding increase of >= 2 points in the fellow eye]) 3 weeks post the fifth infusion (i.e., Week 15)

Secondary outcome

Safety Endpoints

• Adverse Events (AEs) and Serious Adverse Events (SAEs) will be monitored and recorded throughout the duration of the study. All clinically significant changes in other safety measurements will be recorded as AEs.

Key Secondary Endpoints in the USA, Canada and China in the Pivotal portion of the Study (THRIVE):

• Change from baseline in Proptosis in the study eye as measured by exophthalmometer at Week 15

• Clinical Activity Responder Rate in the study eye at Week 15

• Change from baseline in CAS in the study eye at Week 15

• Overall Responder Rate in the study eye at Week 15

• Diplopia Resolution Rate (i.e., reduction in Gorman Subjective Diplopia Score to 0 from baseline for participants with baseline Diplopia Score >0) at Week 15

• Proportion of participants with a CAS score of zero or one in the study eye at Week 15

Key Secondary Endpoints in Australia, EU and UK in the Pivotal portion of the Study (THRIVE):

• Change from Baseline in proptosis in the studyeye as measured by exophthalmometer at Week 15

• Change from baseline in CAS in the study eye at Week 15

• Diplopia Resolution Rate at (i.e., reduction in Gorman Subjective Diplopia Score to 0 from baseline for participants with baseline Gorman Subjective Diplopia Score >0) Week 15

• Proportion of participants with a CAS score of zero or one in the study eye at Week 15

Exploratory Endpoints in Australia, Canada, China, EU, UK and USA in the Pivotal portion of the Study (THRIVE):

• Proptosis Responder Rate in the study eye as measured by exophthalmometer) at Week 24 (12 weeks post fifth infusion), Week 36 (24 weeks post fifth infusion) and Week 52

• Proptosis Responder Rate in the fellow eye (i.e., reduction of proptosis of >= 2 mm from baseline as measured by exophthalmometer) at Weeks 15, 24, 36 and 52

• Durability of Proptosis Response in the study eye at Weeks 24, 36 and 52

• Time to First Proptosis Response in the study eye

• Clinical Activity Responder Rate in the study eye at Weeks 24, 36 and 52

• Clinical Activity Responder Rate in the fellow eye at Weeks 15, 24, 36 and 52

• Change from baseline in CAS in the study eye at Weeks 24, 36 and 52

• Change from baseline in CAS in the fellow eye at Weeks 15, 24, 36 and 52

• Time to first CAS Response in the study eye

• Overall Responder Rate in the study eye at Weeks 24, 36 and 52

• Overall Responder Rate in the fellow eye at Weeks 15, 24, 36 and 52

• Time to First Overall Response in the study eye

• Diplopia Resolution Rate at Weeks 24, 36 and 52

• Proportion of participants with a CAS score of zero or one in the study eye at Weeks 24, 36 and 52

• Proportion of participants with a CAS score of zero or one in the fellow eye at Weeks 15, 21, 36 and 52

• Proptosis Response Rate in the study eye as measured by magnetic resonance imaging [MRI] or Computed Tomography [CT - where allowed by local health authorities] at Weeks 15, 24, 36 and 52

• Change from baseline in the following parameters at Weeks 15, 24, 36 and 52:

o Proptosis in the study eye by MRI (or CT - where allowed by local health authorities)

o Extraocular muscles in the study eye as determined by MRI (or CT - where allowed by local health authorities)

o Orbital fat in the study eye as measured by MRI (or CT - where allowed by local health authorities)

o Manual measurement of lid retraction in the study eye

o Graves* Orbitopathy-Quality of Life (GO-QoL) combined score

o GO-QoL activity subscale

o GO-QoL appearance subscale

o EQ-5D-5L QoL questionnaire

o Visual Acuity (VA)

o Gorman Subjective Diplopia Score

• VRDN-001, IGF-1 and anti-drug antibodies (ADA) at various time points pre-

and post-infusions

Study description

Background summary

Thyroid Eye Disease (TED) is an autoimmune condition resulting in varied presentations which include dry eyes, increased lacrimation, local irritation and eyelid retraction. As the pathophysiology progresses, signs and symptoms increase to include proptosis, diplopia, restriction of ductions and versions and optic nerve compression, with ensuing vision loss.

This constellation of signs and symptoms causes difficulty with working, driving, reading and other activities of daily living, and leads to psychosocial distress and social withdrawal. Many patients with TED endure at least 5 to 7 years of medical and surgical therapy before reaching a point of stability, transformed physically, emotionally and visually, with overwhelming dysfunction in their quality of life.

Treatment during the active phase of the disease focuses on preserving sight and the integrity of the cornea as well as anti-inflammatory measures. There had been no direct therapy available for the diplopia and proptosis, or periorbital edema and lid retraction.
Current treatments of TED are generally incomplete and unsatisfactory both for the patient and treating physicians. As symptoms and signs become more severe, the only alternatives were extraocular muscle surgery, orbital radiation and orbital decompression. Again, even these interventions were incomplete and often unrewarding.

The principle underlying pathology of TED is the activation of an inflammatory cascade within the orbital cone, primarily due to autoantibodies against the thyroid stimulating hormone receptor (TSHR) which has been shown to exhibit cross talk (transactivation) with the IGF-1R. Transactivation between the TSHR and the IGF-1R forms the basis for the therapeutic use of anti-IGF-1R mAbs in TED.

The anti-IGF-1R approach has proven to be clinically valuable. Teprotumumab, a mAb directed against the IGF-1 receptor, was shown to be effective in reducing proptosis, diplopia and inflammation in patients with active TED. Therefore, VRDN-001, also a mAb directed against the IGF-1 receptor, may provide therapeutic benefit in TED patients.

In this study the safety, tolerability, and efficacy of VRDN-001 are investigated, as well as the pharmacokinetic (PK) and pharmacodynamic (PD) profiles in HV and TED patients over a dose range of 3.0 to 20.0 mg/kg.

The rationale for selecting 5 infusions as the dosing regimen in the active TED pivotal portion of the study (THRIVE) is based on available interim VRDN-001 data and published information for teprotumumab have demonstrated that more than 90% of the proptosis response is observed following the first 5 infusions with minimal further improvement thereafter. Furthermore, in the VRDN-001-101 active TED MAD study, the time to a proptosis response, defined as a reduction from baseline of 2 mm in the study eye (without an increase of 2 mm in the fellow eye) as measured by exophthalmometer, occurred between 3 to 4 weeks compared to the median time of response of 6.4 weeks for teprotumumab. This correlated with the time to a reduction in the clinical signs and symptoms (CAS) to a score of 0 or 1 which also occurred between week 3 and 4 in the VRDN-001-101 active TED MAD study. These results suggest that the required duration of treatment with VRDN-001 may be less than seen with teprotumumab.

Study objective

This study has been transitioned to CTIS with ID 2024-512244-36-00 check the CTIS register for the current data.

The objectives of this are to establish the safety, tolerability, and efficacy of VRDN-001, and the pharmacokinetic (PK) and pharmacodynamic (PD) profiles of VRDN-001 in HV and TED patients over a dose range of 3.0 to 20.0 mg/kg.

Study design

The study design will be randomized, double-masked, and placebo-controlled, where both participants and site personnel (except pharmacy personnel preparing the infusate) will be masked to treatment, and the sponsor will not be masked. The MAD studyparticipants will be comprised of both HVs and participants with TED. In the EU only patients with TED will be included in the study (no healthy volunteers).

Three dose levels will be evaluated in HVs and active TED MAD subjects: 3.0 (low), 10.0 (middle), and 20.0 (high) mg/kg. Each participant will receive two doses administered by intravenous infusions, 3 weeks apart. The low dose cohort will be comprised of 4 NHVs randomized 3:1 (VRDN-001: placebo) and the middle and high dose cohorts will be comprised of 4 HVs and 8 participants with active TED with each group randomized 3:1 (VRDN-001: placebo). An independent Data Safety Monitoring Board (DSMB) will decide on whether dose escalation can occur, from low dose to middle dose and middle dose to high dose, one week after the fourth HV participant at each dose level completes their second infusion. The low dose level will enroll 4 HVs, randomized 3:1 (VRDN-001:

placebo). Two HV subjects (*sentinel* participants) at the low dose level will be treated and followed through 1 week after their first infusion before the next 2 HV low dose participants are treated. If a Dose-Limiting Toxicity (DLT) (defined as an Adverse Event [AE] with a severity >= Grade 3 on the Common Terminology Criteria for Adverse Events [CTCAE] scale [reference Appendix 3 in protocol]) occurs in any of the HV low dose participants receiving active drug, a second cohort of 4 HVs will be enrolled, randomized 3:1 (VRDN 001: placebo), and treated at the low dose to confirm that there are no additional DLTs before dose escalation. In the case of a Grade 4 related toxicity in any participant, the participant will be withdrawn from treatment and the independent Data Safety Monitoring Board (DSMB) will review the data and provide their recommendations. At the middle dose level, in parallel to the safety evaluation in HVs, the study will begin enrolling active TED participants after the first two sentinel HV participants at the middle dose level have been treated and followed for one week following their first dose. If a DLT occurs in any of the HV middle dose participants receiving active drug, then dose escalation will not occur until all 8 active TED participants have been treated without a further DLT. The investigators will be involved in the decision to dose escalate, or not, in conjunction with the DSMB. If dose escalation of the HVs from the middle to the high dose has occurred while the active TED participants continue to be treated at the middle dose level and a second DLT occurs at the middle dose level, then further treatments at the middle and high dose levels will be immediately discontinued and the Maximum Tolerated Dose (MTD) will be considered to be the low dose level. The MTD will be defined as the dose at which not more than 1 DLT occurred and no further treatments will occur at a higher dose level than the MTD. Similarly, at the high dose level, in parallel to the safety evaluation in HVs, the study will begin enrolling active TED participants after the first two sentinel HV participants at the high dose level have been treated and followed for one week following their first dose. If more than one DLT occurs among the HV and active TED participants at the high dose level, the middle dose will be considered the MTD. If the highest dose is selected as MTD, and middle and high doses exhibit similar evidence of clinical activity in terms of proptosis response rate, then 8 active TED participants may be enrolled at the low dose (3.0 mg/kg) and based on those data a further cohort of 8 active TED participants may also be enrolled at a low-intermediate dose (5.0 mg/kg), with both cohorts randomized 3:1 (VRDN-001:placebo), in order to establish a dose response curve for clinical activity.

Two additional cohorts of participants with chronic TED (defined as those participants with symptoms of TED occurring more than 1 year prior to entry to the study), will also be enrolled and treated with 10 mg/kg VRDN-001 and another dose (to be selected following the results of the active TED MAD cohorts), respectively. Both cohorts will be randomized 3:1 (VRDN-001: placebo), and the cohorts may be enrolled sequentially at any time after completion of enrollment of the 20 mg/kg active TED MAD cohort.

The HV and Active TED MAD portions of the study have been completed. The Chronic TED MAD portion of the study is fully recruited but remains active.

The pivotal portion of the (THRIVE) will be a randomized, double-masked (including the sponsor) and placebo-controlled study in active TED participants whose signs and symptoms declared themselves within 15 months of screening. The dose selected is 10mg/kg (which is half the maximum tested dose in the active TED MAD portion of the study). The study will be comprised of 90 participants (to ensure 78 evaluable participants at the primary endpoint at 3 weeks post the fifth infusion (i.e., Week 15) randomized with an allocation ratio of 2:1, (60 participants active: 30 participants placebo), stratified at baseline by level of proptosis (> or equal to 23 mm, Y/N), and will compare the efficacy of 5 infusions of 10 mg/kg VRDN-001 administered at 3-week intervals to placebo.

Participants in the pivotal portion of this study (THRIVE) were either randomized (1:1:1) to 5 infusions or 8 infusions versus placebo (as per all previous versions 7.0 and before of the VRND-001-101 protocol) or will be randomized (2:1) to 5 infusions versus placebo, since version 8.0 of the protocol), each administered as IV infusions at 3- week intervals. All participants will receive a total of 5 to 8 infusions to maintain masking as determined by the protocol version to which the participants were randomized. For participants previously randomized to 8 infusions and who have received greater than 5 infusions, further infusions will be discontinued. The active TED Pivotal portion of the trial is ongoing.

Participants who are deemed to be non-responders at 3 weeks post the fifth infusion (i.e., Week 15) in the pivotal portion of the study may be offered the option to enroll into an open-label treatment study where they will receive 5 further infusions of VRDN-001 at 3-week intervals for a further 12 weeks of treatment. For some countries, per local health authority requirements participants may be unmasked prior to the decision to enroll in the open-label treatment study. A non-responder is defined as either:
*A participant who did not achieve a >= 2 mm reduction from baseline in proptosis (as measured by exophthalmometer) in the study eye at 3 weeks post the fifth infusion (i.e., Week 15)
OR
*A participant who achieved a >= 2 mm reduction from baseline in proptosis (as measured by exophthalmometer) in the study eye but had a corresponding increase of >= 2 mm from baseline in proptosis in the fellow eye at 3 weeks post the fifth infusion (i.e., Week 15).

The Day-1/Day 1 visit(s) in the open-label treatment study (separate study denoted as VRDN-001-302) are to be conducted within 4 weeks of the 3 weeks post the fifth infusion assessment (i.e., Week 15) in the VRDN-001-101 pivotal study (THRIVE). More than 4 weeks may be allowed between the completion of the 3 weeks post the fifth infusion assessment (i.e., Week 15) in the piotal study and the Day-1/Day 1 visit of the open-label treatment study with prior written

approval by the Sponsor.

Measurements will continue to be collected through 52 weeks for those participants who are deemed to be responders (i.e., did achieve a >=2 mm reduction in proptosis in the study eye as measured by exophthalmometer) at 3 weeks post the fifth infusion (i.

Intervention

Three dose levels will be evaluated in HVs and active TEDMAD participants. One group receives an IV infusion twice with VRDN-001 in one of the following doses: 3.0 (low), 10.0 (middle), and 20.0 (high) mg/kg. Each participant will receive two doses administered by intravenous infusions, 3 weeks apart. The other group receives an IV infusion twice as well, with placebo (saline).Participants in the pivotal portion of this study (THRIVE) were either randomized (1:1:1) to 5 infusions or 8 infusions versus placebo or will be randomized (2:1) to 5 infusions versus placebo, each administered as IV infusions at 3- week intervals. For participants previously randomized to 8 infusions and who have received greater than 5 infusions, further infusions will be discontinued.

VRDN-001 is a humanized mAb directed to IGF-1R. VRDN-001 will be provided as a solution containing 25 mg/mL or 50 mg/mL of antibody in 4.0 mL extractable volume in 10R vials, frozen at -20 ± 5oC.

The pharmacist or other qualified, trained and delegated individual preparing the infusion bags will be unmasked to treatment and will either dispense 100 mL (low dose cohort), or 250 mL (middle and high dose cohorts) bags of saline with or without VRDN-001 added, according to the Randomization and Trial Supply Management (RTSM) System. The volume of saline removed from the bags will equal the volume of VRDN-001 added to maintain masking. In the MAD study the bags will be infused at 2.8 mL per minute which approximates to 36 (±10) and 90 (±15) minutes for the 100 mL and 250 mL bags, respectively. In the pivotal portion of the study, the 250 mL bags will be infused at 2-3 mL per minute for the first 15 minutes, then advancing to 8-9 mL per minute thereafter, for the first infusion which approximates to 40 (±10) minutes. Each subsequent infusion will be infused at 8-9 mL per minute which approximates to 30 (±10) minutes for the total infusion.

Study burden and risks

Burden:
Subjects will need to undergo the following procedures/tests:
- IV infusion with study drug (250 ml), mildly invasive, 2 times for MAD cohort and 5 times for Pivotal cohort, duration max. 90 min.

- eye examinations, mildly invasive, 6 times (MAD cohort) or 10 times (Pivotal cohort)
- eye/facial MRI, mildly invasive, 4 times for MAD cohort and 5 times for Pivotal cohort.
- Venapunctures: 11 times (incl 8 PK samples) for MAD cohort or 16 times (incl. 22 PK samples) for Pivotal cohort (41 ml per occasion)
- Physical examination: 2 times (both cohorts)
- Vital signs and ECG: 10 times (MAD cohort) or 23 times (Pivotal cohort)
- Questionnaire: 6 times (MAD cohort) or 10 times (Pivotal cohort)
- Facial photography to assess gaze: 4 times (both cohorts)
- Hearing test: 5 times (MAD cohort) or 10 times (Pivotal cohort)

Other relevant instructions/behavioral rules are:
- Use appropriate measures to avoid pregnancy (both male and female participants), if applicable
- Fasted visits: 2 times for MAD cohort and 5 times for Pivotal cohort (mornings of the IV infusions with study drug).

Risks:
Risks involved are possible side-effects of the study drug, as well as discomforts as a result of study assessments.
The potential risks of VRDN-001 include:
• Muscle cramps or spasms
• Nausea
• Diarrhea
• High blood sugar
• Hearing impairment including hearing loss
• Headache
• Fatigue
• Dry skin
• Altered sense of taste
• Hair loss
• A reaction at the site of intravenous infusion
• Worsening of inflammatory bowel disease
• Menstrual Disorders

The following study assessments may cause discomforts for subjects:
• Eye assessments (intraoculair pressure measurement, slit lamp biomicroscopy and fundoscopy and lid retraction measurement)
• MRI
• Blood drawing

Benefit:
TED is generally recognized as a disease with major impact on the lives of patients suffering form it. Current treatments of TED are generally incomplete and unsatisfactory. Many patients with TED, when reaching a point of stability after years of treatment, are transformed physically, emotionally and visually, with overwhelming dysfunction in their quality of life.

VRDN-001, as an mAb directed against the IGF-1 receptor, may provide therapeutic benefit in TED patients. However, there is no guarantee that participation in the current study will help the participant; the participant may receive a placebo treatment.

Risk-benefit analysis:
Considering the nature of the disease and its major impact on the lives of patients suffering from it, and current lack of appropriate treatment options, as well as taking into account the measures taken to minimize risk to participants taking part in this study, the potential risks identified in association with VRDN-001 are justified by the anticipated benefits that may be afforded to participants with TED.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion Criteria:
Enrollment in the HV and Active TED MAD cohorts has been completed.
The inclusion criteria corresponding to the HV and Active and Chronic TED MAD cohorts are now described in Appendices 4 and 5 (Protocol V8.0), respectively.

Active TED Pivotal (THRIVE) participants
Participants must:
1. Be able to understand the study procedures and the risks involved and be willing to provide written informed consent before the first study-related activity
2. Be an adult male or female participant, at least 18 years of age or older
3. Have had a clinical diagnosis of TED with a CAS of >= 3 on the 7-item scale for the study eye
4. Have moderate to severe (i.e., has an appreciable impact on daily living) active TED associated with proptosis of >=3 mm above normal values for race and gender in the opinion of the investigator and at least one of the following: lid retraction of >=2 mm, moderate or severe soft tissue involvement, periodic or constant diplopia, spontaneous retrobulbar pain or pain on eye movement, swelling of the conjunctiva, eyelids or plica, or redness of the eyelids or plica in the study eye
5. Have documented evidence of ocular symptoms or signs associated with active TED that began within 15 months prior to study screening
6. VRDN-001 can be started concomitantly with attempts to achieve euthyroid status. Underlying thyroid status is not an inclusion criterion.
7. Not require expected immediate surgical ophthalmological or orbital surgery in the study eye for any reason
8. VRDN-001 can be used with caution in patients with diabetes mellitus. Diabetic participants should be monitored by their endocrinologist or other appropriately trained personnel and have at study entry a glycated hemoglobin (HbA1c) of <8.5%
9. If female, have a negative serum pregnancy test at screening and further negative urine tests immediately before each dose of study medication following the last dose of study medication as described in Appendix 1C if the participant is a woman of childbearing potential (including those with <2 years since the onset of menopause, amenorrhea for <1 year, or not surgically sterile); such participants must agree to use an acceptable method of contraception such as a condom and a second highly effective method of contraception as described in Section 4.4 from Screening up to and including 100 days after the last dose of study medication. If the participant is initiating hormonal contraception at time of Screening or within one cycle of Day 1, participant agrees to use a double-barrier method of contraception until completing one-full cycle of hormonal contraception. An acceptable double-barrier combination method is a condom with either diaphragm or sponge with spermicide

10. Be surgically sterile males for at least 6 weeks, or agree to use an acceptable method of contraception such as a condom and a second highly effective method of contraception as described in Section 4.4 from Screening up to and including 100 days after the last dose of study medication
11. Be willing and able to comply with all the requirements of the protocol for the entire duration of the study

Exclusion criteria

Exclusion Criteria
Enrollment in the HV and Active TED MAD cohorts has been completed.
The exclusion criteria corresponding to the HV and Active and Chronic TED MAD cohorts are now described in Appendices 4 and 5 (Protocol V8.0), respectively.

Active TED Pivotal (THRIVE) participants
Participants must not:
1. Have received prior treatment with another anti-IGF-1R therapy or any investigational agent for TED
2. Have a compressive optic neuropathy of TED that is expected to require surgical decompression in the immediate future.
3. Have corneal decompensation in the study eye unresponsive to medical management
4. Have a decrease in CAS of >=2 points in the study eye between screening assessment and Day -1
5. Have a decrease in proptosis of >=2 mm in the study eye between screening assessment and Day -1
6. Have had previous orbital irradiation or decompression surgery involving excision of fat for TED to the study eye*s orbit
7. Have history of or screening audiometry assessment of significant (as determined by the Investigator) ear pathology, relevant ear surgery or hearing loss
8. Have inflammatory bowel disease (e.g., biopsy proven or clinical evidence of inflammatory bowel disease)
9. Have used systemic corticosteroids for any condition, including TED, or selenium within 2 weeks prior to the first dose of study medication (topical steroids or multivitamins that contain selenium are permitted)
10. Have received other immunosuppressive agents, including rituximab, or tocilizumab, for any condition, including TED, within 8 weeks prior to the first dose of study medication
11. Have received any other therapy for TED within 8 weeks prior to the first dose of study medication (artificial tears are permitted)
12. Have received an investigational agent for any condition within 8 weeks prior to the first dose of study medication
13. Have a pre-existing ophthalmic condition in the study eye which in the opinion of the Investigator, would confound interpretation of the study results

14. Be a pregnant or lactating woman
15. Be an active alcoholic or illicit drug user or considered at high risk of relapse by the Investigator
16. Have a known hypersensitivity to any of the components of VRDN-001 or placebo formulations, or prior hypersensitivity to monoclonal antibodies (mAbs)
17. Have any condition, which in the opinion of the Investigator, would preclude inclusion in the study
18. Have a positive test for human immunodeficiency virus (HIV-1 and HIV-2)
19. Have a positive test for active hepatitis B or hepatitis C infection
20. Have previously participated in this study or any study of VRDN-001
21. French participating sites only: In accordance with the provisions of articles L.1121-5 et seq. of the Public Health Code, pregnant or breastfeeding women, persons deprived of their liberty by a judicial or administrative decision, persons under psychiatric care without their consent, minors and adults under a legal protection measure must not be included

Note: Prior thyroidectomy, radioactive iodine (RAI) treatment, or orbital decompression surgery limited to bone only are NOT exclusions.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-08-2023
Enrollment:	6
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	VRDN-001
Generic name:	VRDN-001

Ethics review

Approved WMO Date:	14-04-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-08-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-09-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-05-2024
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-08-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-512244-36-00
EudraCT	EUCTR2021-006794-37-NL
ClinicalTrials.gov	NCT05176639
CCMO	NL80863.078.22