

# VRDN-001, a Full Antagonist Antibody to IGF-1 Receptor in Development for Thyroid Eye Disease (TED): Pharmacodynamic Responses in Healthy Volunteers and Patients with Active TED

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## KEY TAKEAWAYS

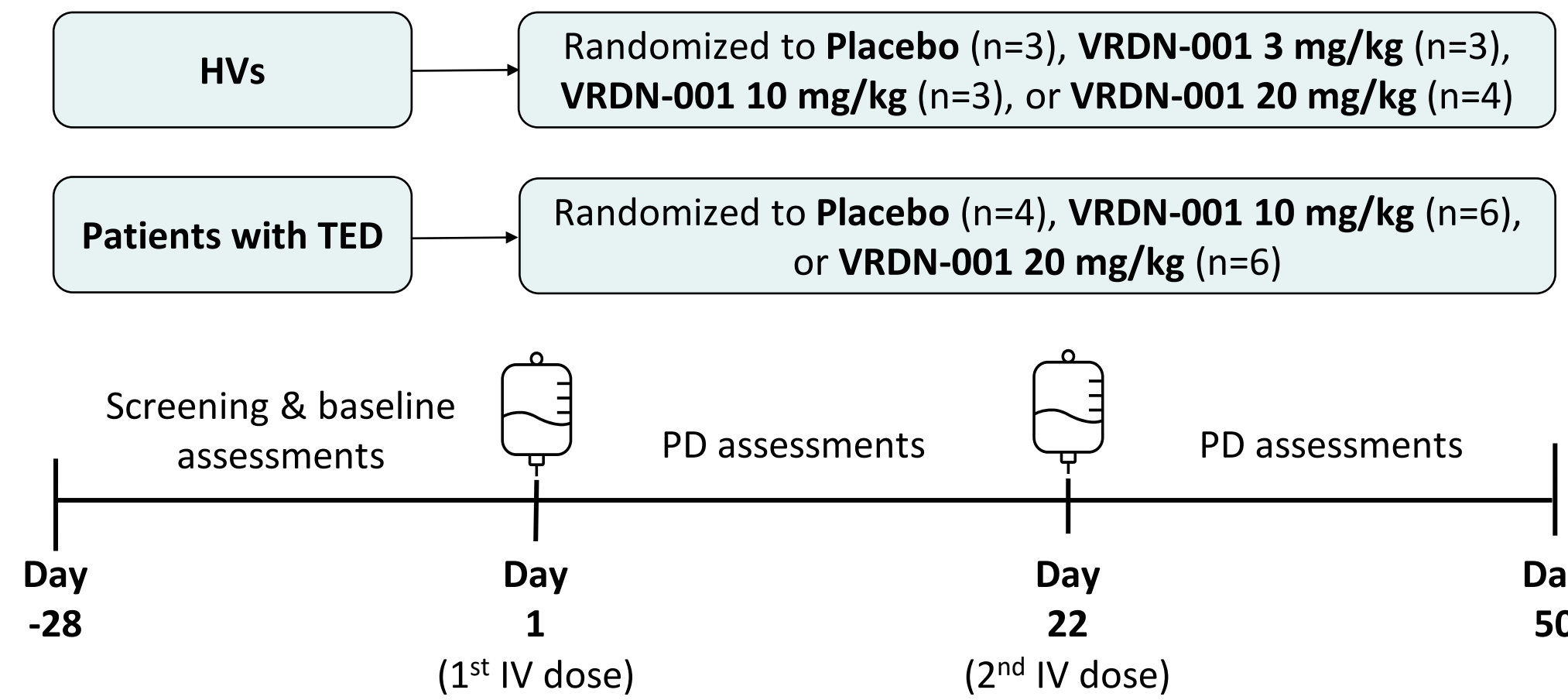
Pharmacodynamic (PD) results from our ongoing placebo-controlled phase 1/2 trial in healthy volunteers (HVs) and patients with active TED treated with 2 infusions of VRDN-001:

- VRDN-001 elicited rapid and sustained increases in IGF-1 serum levels that were similar across groups, indicating maximal target engagement at all doses tested.
- All doses were generally well tolerated, with no severe or serious AEs or infusion reactions observed.
- In HVs receiving 3-20 mg/kg VRDN-001, mean IGF-1 serum levels increased 5-7-fold from baseline.
- In patients with TED receiving 10 or 20 mg/kg VRDN-001, mean IGF-1 serum levels increased 6-fold from baseline.

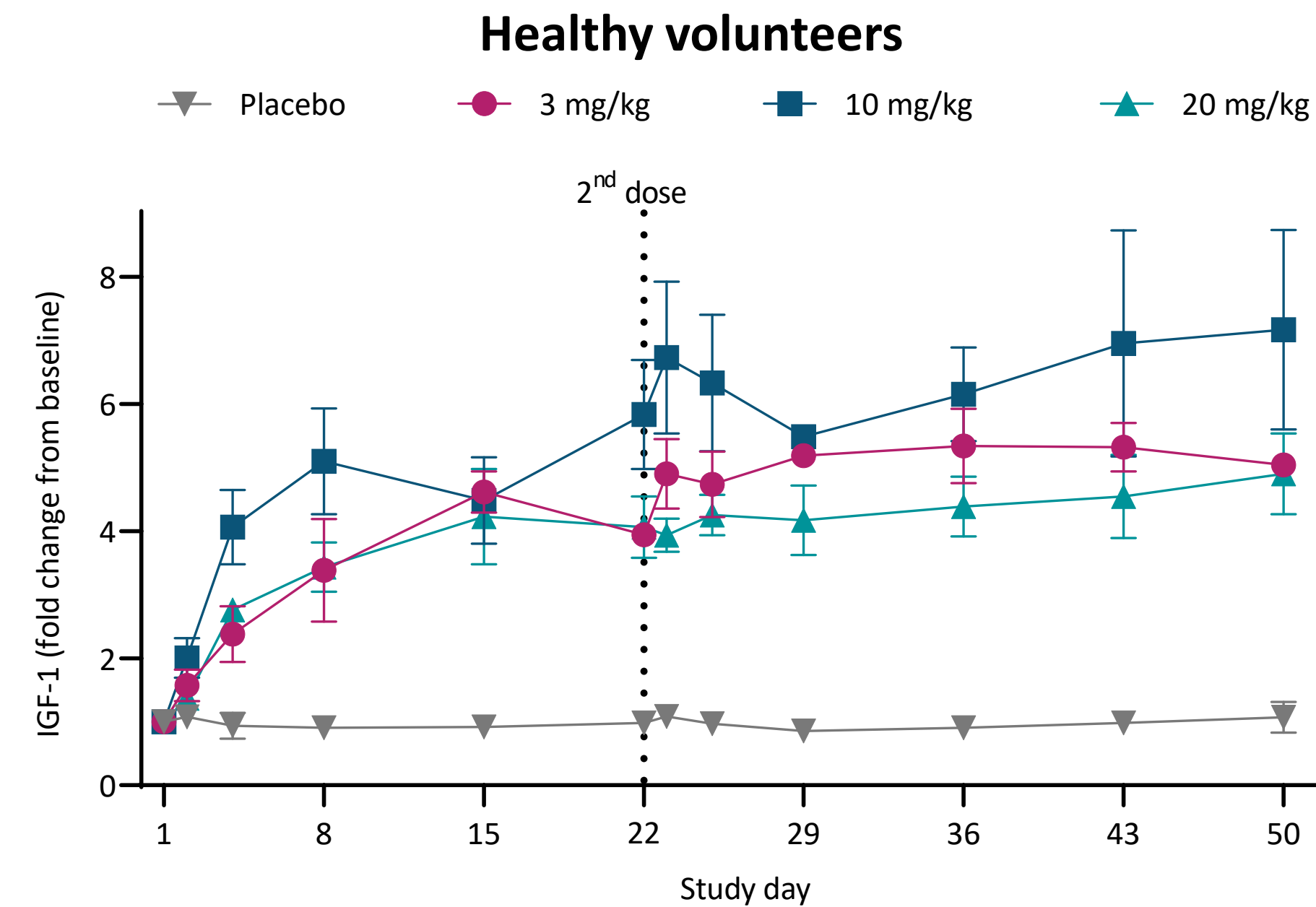
The efficacy and safety of VRDN-001 for the treatment of TED will be further assessed in the ongoing THRIVE phase 3 clinical trial (NCT05176639).

## INTRODUCTION AND STUDY DESIGN

- VRDN-001, a full antagonist antibody to the IGF-1 receptor, is under development for the treatment of TED.
- Clinical and preclinical evidence suggest a central role for IGF-1 receptor antagonism in reducing the inflammation and proptosis that occur in TED.<sup>1-3</sup>
- We assessed the PD response (serum IGF-1 levels) to treatment with VRDN-001 in HVs and patients with active TED through 50 days.



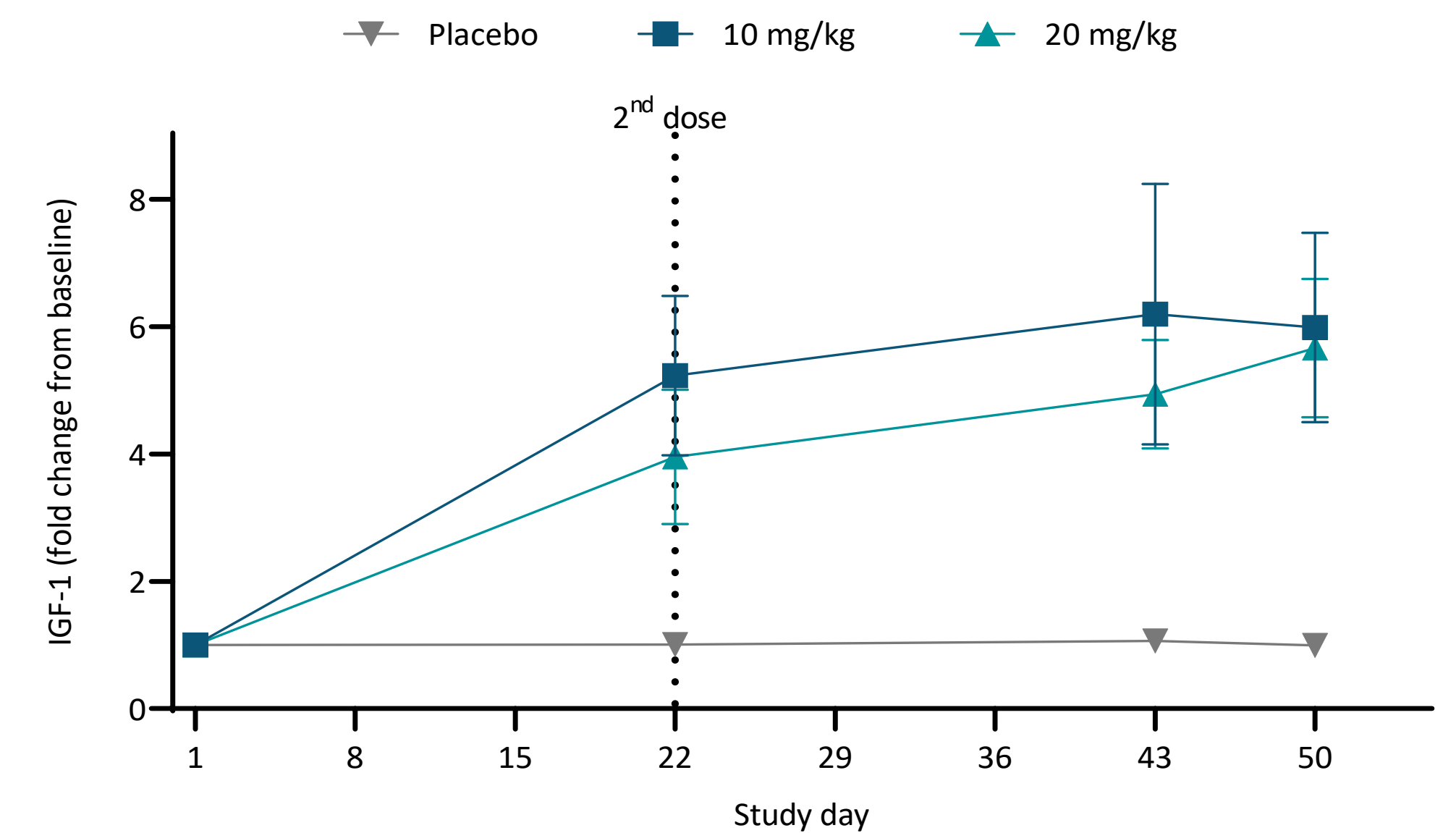
## VRDN-001 INCREASES IGF-1 SERUM LEVELS



Data are mean and SD. Missing baseline samples were normalized to population baseline average. Data from the withdrawn participant (20 mg/kg) are included for the 1<sup>st</sup> dose.

- Mean IGF-1 levels across the VRDN-001 groups increased from 95-143 ng/mL at baseline to 655-685 ng/mL after 2 infusions, representing a 5-7-fold increase.
- Increases occurred within a day of the first infusion and were sustained through 50 days.

## Patients with active TED



Data are mean and SD.

- Mean IGF-1 levels in patients with TED across the VRDN-001 groups increased from 139-156 ng/mL at baseline to 853-907 ng/mL after 2 infusions, representing a 6-fold increase.
- Increases occurred after the first infusion and were sustained through 50 days.

## STUDY PARTICIPANTS

- Adult HVs and patients with active, moderate-to-severe TED were randomized to receive 2 intravenous infusions 3 weeks apart of either placebo or VRDN-001.
- In the HV cohorts (n=13), 12 HVs completed the trial; 1 in the 20 mg/kg group withdrew for personal reasons after the 1<sup>st</sup> infusion and was followed through Day 35. Mean age was 49 years; 8 were male and 5 were female.
- In the TED cohorts (n=16), all patients completed the trial. Mean age ranged from 39 to 49; 3 were male and 13 were female.

## THERAPEUTIC IMPLICATIONS

- Increased serum levels of IGF-1 induced by VRDN-001 in HVs and patients with TED are consistent with the 6-fold IGF-1 increases induced by VRDN-001 in oncology patients<sup>4</sup> and indicate maximal target engagement, even at the lowest dose.
- Preliminary results from a phase 2 proof-of-concept study of 2 infusions of either 3, 10, or 20 mg/kg VRDN-001 in patients with active TED is presented in Poster# FRI-545.
- The efficacy and safety of VRDN-001 for the treatment of TED will be further assessed in the ongoing THRIVE phase 3 clinical trial (NCT05176639).



Poster# FRI-545



Poster# FRI-546

**Disclosures:** This study was sponsored by Viridian Therapeutics Inc. VRDN-001 is an investigational therapy not approved in any country. Formatting and editorial assistance was provided by Keira Kim, an employee of Viridian Therapeutics Inc. All authors met the ICMJE authorship criteria and had full access to relevant data. The authors would like to thank the study investigators, research teams, and study participants who make this research possible.

**References:** 1. Pritchard J et al. *J Immunol*; 170:6348–6354 (2003); 2. Krieger CC et al. *J Clin Endocrinol Metabolism*; 100:1071–1077 (2015); 3. Smith TJ et al. *NEJM*; 376:1748–1761 (2017); 4. Soria et al. *Eur J Cancer*; 49:1799–1807 (2013).

**PDF of poster and additional information:** Scan QR code

**Abbreviations used in poster:** IGF-1R, insulin-like growth factor-1 receptor; HV, healthy volunteer; PD, pharmacodynamic; IV, intravenous; SD, standard deviation

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