

An open-label, Phase 1b study to assess the safety, tolerability, and efficacy of TX2100 in participants with hematologic support-dependent hereditary hemorrhagic telangiectasia (HHT)

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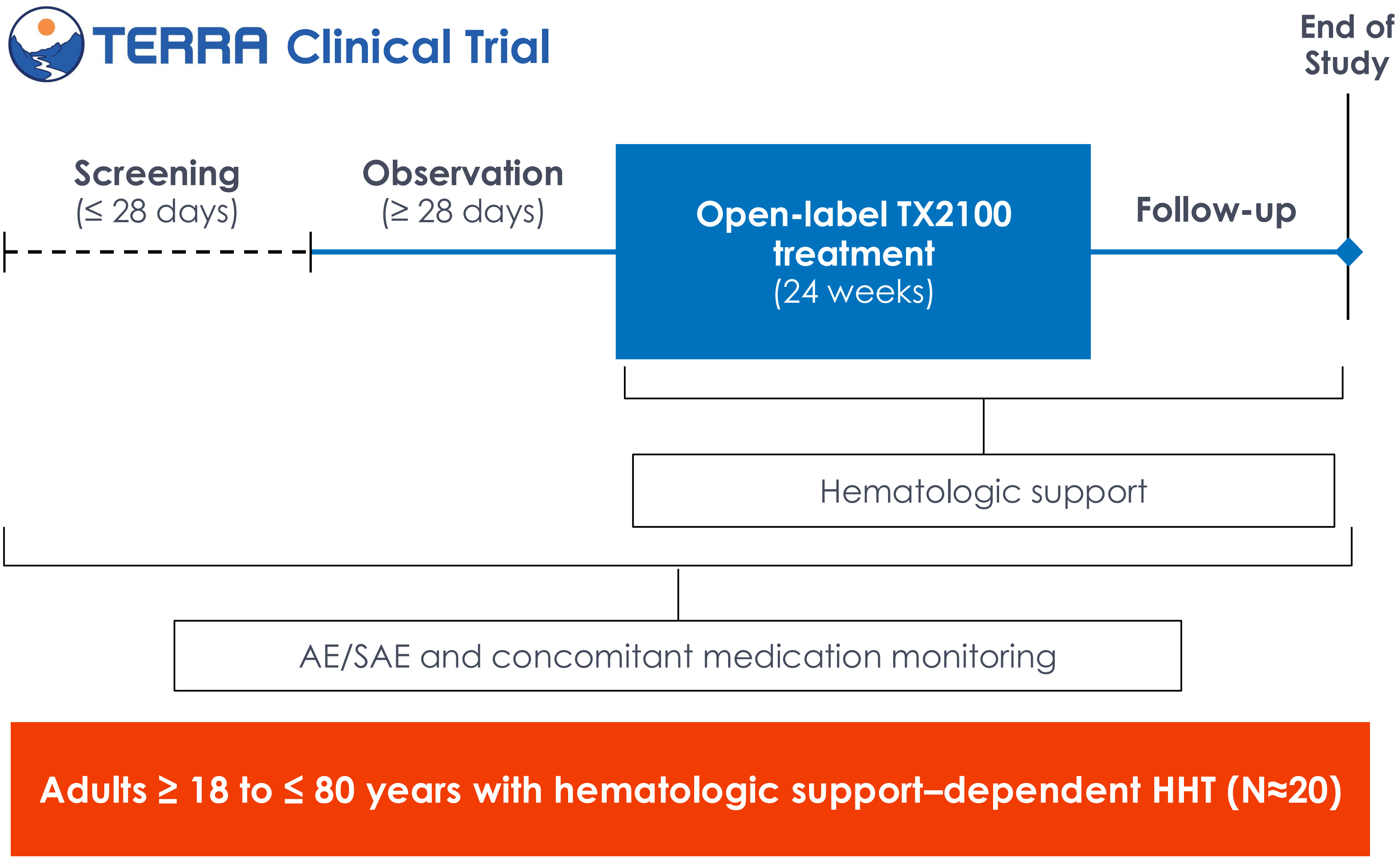
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BACKGROUND

- HHT is the second most common inherited bleeding disorder¹ and has no approved therapies.
- Chronic blood loss from HHT-related bleeding often causes iron-deficiency anemia requiring IV iron infusion and/or RBC transfusion.
- HHT is caused by mutations that disrupt BMP signaling and drive abnormal blood vessel formation (dysangiogenesis)².
- This disrupted signaling upregulates apelin/APJ, a G-protein-coupled receptor signaling pathway in endothelial cells that plays a key role in dysangiogenesis.
- TX2100 is an anti-APJ VHH-Fc antagonist designed to reduce the dysangiogenesis underlying HHT through a mechanism distinct from other agents in clinical development.
- A surrogate APJ antagonist reduced hypervascularization, AVM formation, bleeding, and anemia in HHT mouse models⁵, supporting the mechanistic rationale for TX2100.
- TX2100 has shown a favorable safety and pharmacokinetic profile in an ongoing first-in-human study in healthy participants.⁶
- Study TX2100-002 evaluates the safety, tolerability, and efficacy of TX2100 in participants with hematologic support-dependent HHT.

STUDY DESIGN & SCHEMA



METHODS

- Open-label, multinational Phase 1b study; ~20 participants
- 4 periods: Screening (≤ 28 days) → Observation (≥ 28 days) → 24-week Open-label Treatment → Follow-up (through EOS)
- Key eligibility: age ≥ 18 – ≤ 80 y with HHT³; hematologic support-dependent⁴ (defined by RBC transfusion and IV iron requirements)
- Dosing: TX2100 SC once weekly for 24 weeks
- Assessments: Hematologic support requirements and hematologic parameters, AEs/SAEs, PK

OBJECTIVES & ENDPOINTS

Table 1. Selected Objectives and Endpoints

OBJECTIVE	ENDPOINT(S)
Primary	
Assess the safety and tolerability of TX2100 in participants with hematologic support-dependent HHT	Incidence of AEs/SAEs
Key Secondary	
Explore the effect of TX2100 on composite hematologic support requirements and hemoglobin after 24 weeks of treatment	HSS change from baseline to EOT; HIS at EOT; Hemoglobin change from baseline to EOT
Secondary	
Explore the effect of TX2100 on hematologic parameters and support requirements after 24 weeks of treatment	Change from baseline to EOT in parenteral iron infused, pRBCs transfused, and hematocrit
Describe the concentration of TX2100 in participants with HHT	Serum concentrations of TX2100

CONCLUSIONS

- TX2100-002 is the first study evaluating an APJ antagonist in participants with hematologic support-dependent HHT, a population with no approved therapies.
- The study will explore safety, tolerability, and efficacy of TX2100 in this population with a high unmet need.
- Changes in transfusion and iron needs will be assessed.
- Long term extension clinical trial is planned.

STUDY INFORMATION AND ACKNOWLEDGMENTS

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Disclosures: All authors are current or former employees of Tectonic Therapeutic and may hold stock or stock options.

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Abbreviations: AE/SAE, adverse event/serious adverse event; APJ, apelin receptor; AVM, arteriovenous malformation; BMP, bone morphogenetic protein; EOS, end of study; EOT, end of treatment; HHT, hereditary hemorrhagic telangiectasia; HIS, Hematologic Impact Score; HSS, Hematologic Support Score; IV, intravenous; PK, pharmacokinetic; pRBC, packed red blood cell; RBC, red blood cell; SC, subcutaneous(y); VHH-Fc, variable heavy-chain domain (VHH) Fc-fusion protein.