

An Open-Label Study Evaluating the Pharmacokinetics, Pharmacodynamics, Efficacy, and Safety of Tanruprubart (ANX005) Single Dose in Participants From North America and Europe With Guillain-Barré Syndrome

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Introduction

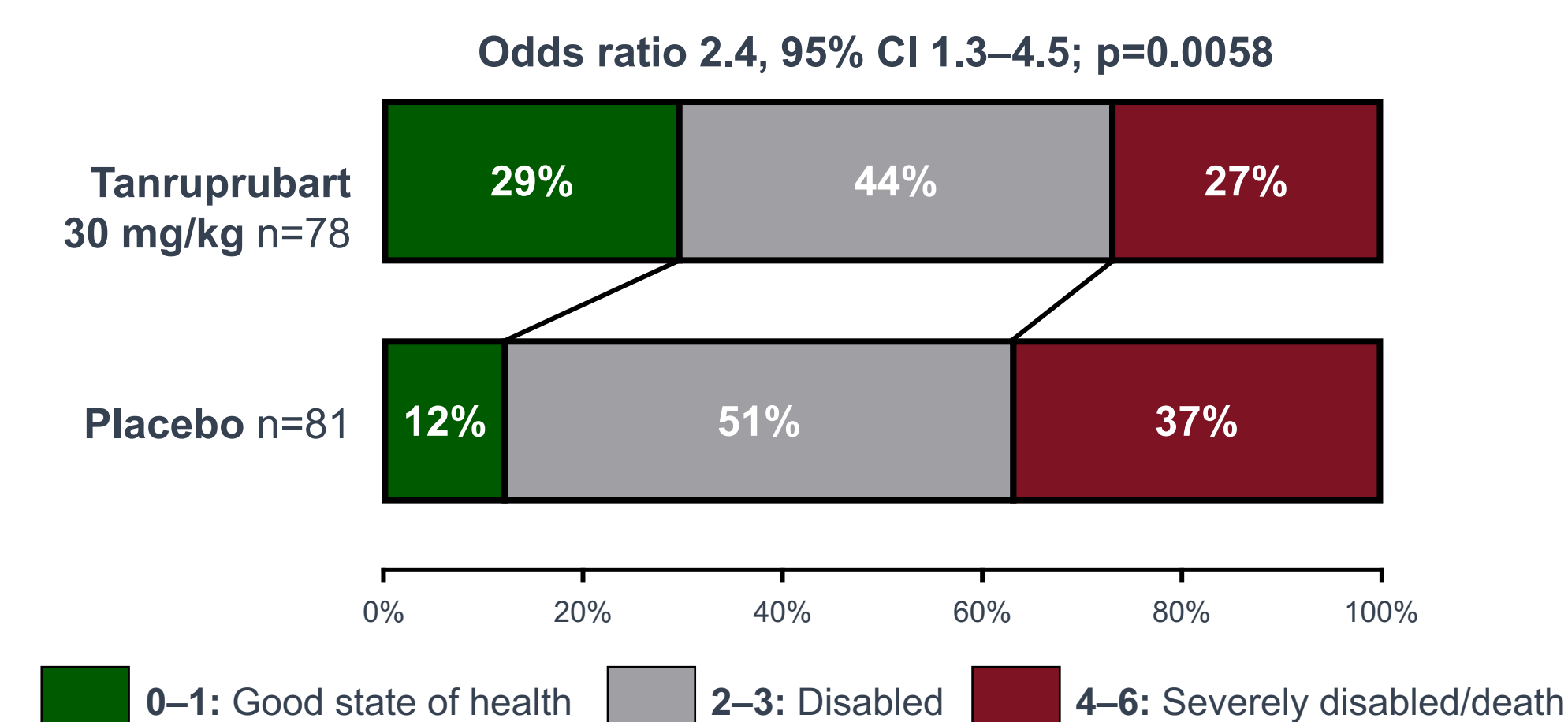
- Guillain-Barré syndrome (GBS) is a rare, acute-onset, life-threatening neuromuscular condition that occurs worldwide and requires immediate intervention.¹
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively and fully blocks C1q, the initiating molecule of the classical complement pathway, thus providing rapid and complete inhibition of classical complement activity to halt neuroinflammation and nerve damage.^{2,3}
- The primary goal of this open-label study (GBS-FORWARD) is to characterize the pharmacokinetics (PK), pharmacodynamics (PD), efficacy, and safety of tanruprubart in participants with GBS in North America and Europe (Figure 1). ClinicalTrials.gov: NCT07020819.

Previous findings

GBS-02

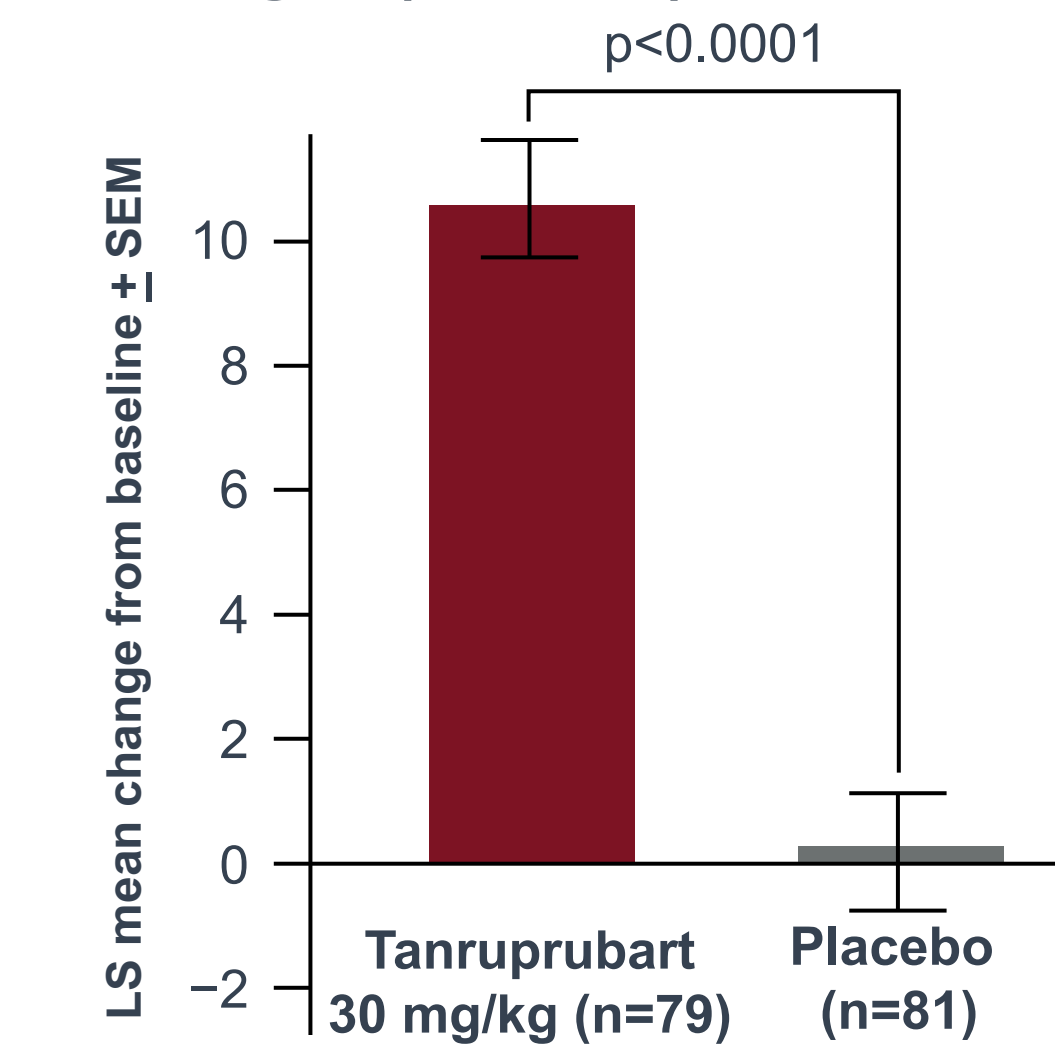
- GBS-02 (NCT04701164) was a Phase 3, multi-center, double-blind, placebo-controlled study of tanruprubart in patients with GBS in Bangladesh and the Philippines.⁴
- This study met the primary endpoint and demonstrated that patients treated with tanruprubart 30 mg/kg had better outcomes (odds ratio 2.4, 95% CI 1.3–4.5; p=0.0058) according to the GBS-disability scale (GBS-DS) relative to placebo at Week 8 (Figure 2), alongside significantly reducing the duration of ventilation over time (p=0.0356).⁴
- Tanruprubart 30 mg/kg led to rapid recovery of muscle strength and motor function, with >10-point improvement in muscle strength based on the Medical Research Council sumscore (MRCss; Figure 3). Also, 87% of participants treated with tanruprubart achieved ≥1-point increase in MRCss from baseline in the first week of treatment, compared with 46% in the placebo group (p<0.0001).
- GBS-DS and MRCss were significantly improved in a broad spectrum of patients, including those with axonal (acute motor axonal neuropathy; AMAN) or demyelinating disease (acute inflammatory demyelinating polyneuropathy; AIDP).⁵
- In study GBS-02, tanruprubart was well tolerated, and most adverse events were mild to moderate in severity, due to GBS and not considered related to study drug. Infusion-related reactions were mostly transient rash; cases were mostly mild to moderate and resolved without sequelae.⁴

Figure 2. GBS-02 primary endpoint: Change in GBS-DS at Week 8



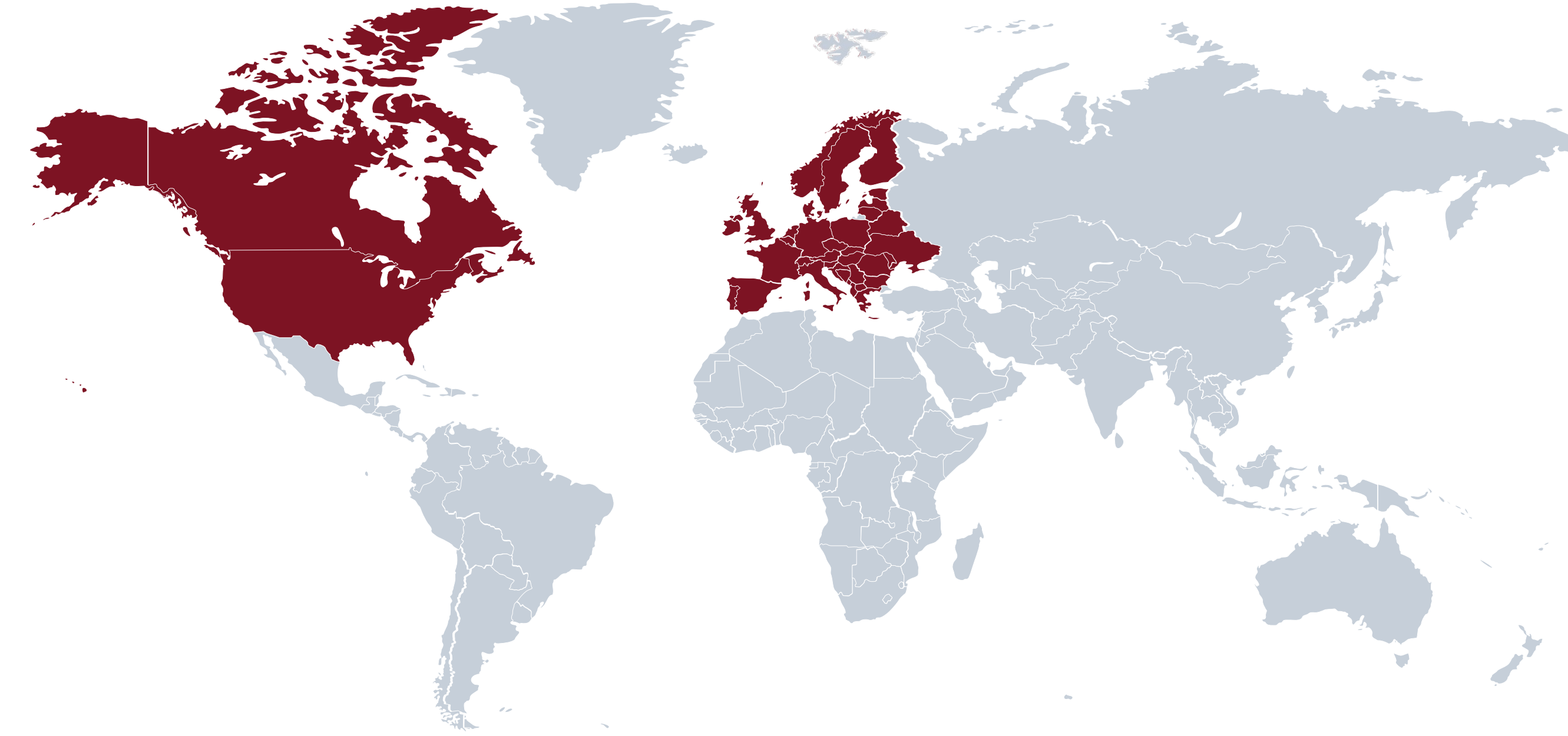
CI, confidence interval.

Figure 3. Recovery in muscle strength (MRCss) at Week 1



LS: Mean point improvement relative to placebo. SEM, standard error of the mean.

Figure 1. Countries participating in the GBS-FORWARD study



Methods and key eligibility criteria

- GBS-FORWARD is a multi-center, open-label, single-arm, PK, PD, efficacy, and safety study of a single intravenous (IV) administration of tanruprubart 30 mg/kg in participants recently diagnosed with GBS.
- 30 participants between the ages of 12 and 85 years will be recruited.
- All participants will receive best supportive care.
- IV immunoglobulin (IVIG) or plasma exchange may be administered in the event of clinical deterioration judged by the investigator and considering these criteria:
 - An unanticipated development of respiratory failure.
 - A ≥5-point worsening from baseline in MRCss.
 - A worsening in GBS-DS ≥1 point from prior visit.

Inclusion criteria

- Diagnosis of GBS according to the National Institute of Neurological Disorders and Stroke Diagnostic Criteria for GBS, including AMAN, or acute motor and sensory axonal neuropathy.
- Onset of GBS-related weakness ≤10 days before start of infusion on Day 1.
- GBS-DS score of 3, 4, or 5 at screening and before start of infusion on Day 1.

Exclusion criteria

- Previous or intended treatment with either IVIG or plasma exchange for GBS.
- Diagnosis of a variant of GBS, including Miller Fisher syndrome, Bickerstaff's encephalitis, and overlap syndromes.

CONCLUSIONS

- In study GBS-02, C1q inhibition with tanruprubart significantly improved the odds of being in a better state of health in participants from Bangladesh and the Philippines.⁴
- This open-label study (GBS-FORWARD) will recruit participants with recently diagnosed GBS in North America and Europe to confirm the generalizability of previous study findings.
- This study aims to add to the current body of evidence demonstrating the efficacy, safety, and tolerability of tanruprubart (30 mg/kg) in patients with GBS.

References
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