004

An Open-Label Study (FORWARD) 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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For more information on GBS-FORWARD

Introduction

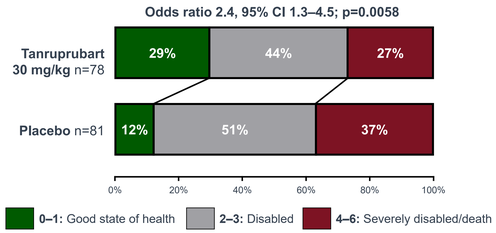
- Guillain-Barré syndrome (GBS) is a rare, acute-onset, life-threatening neuromuscular condition that occurs worldwide and requires immediate intervention[1]
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively and fully blocks C1q, the initiating molecule of the 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

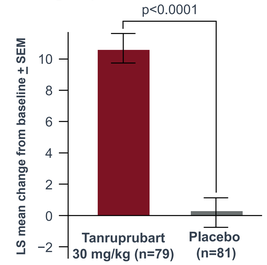
- GBS-02 (NCT04701164) was a Phase 3, multi-center, double-blind, placebo-controlled study of tanruprubart in patients with GBS in Bangladesh and the Philippines[4]
- This study met the primary endpoint and demonstrated that patients treated with tanruprubart 30 mg/kg had better outcomes (odds ratio 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, the most common adverse event, were mostly transient rash; cases were mostly mild to moderate and resolved without sequalae[4]

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



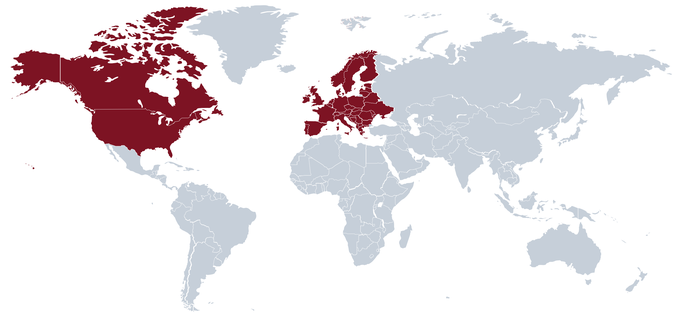
CI, confidence interval.

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



LS: Mean point improvement relative to placebo.
LS, least squares; 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 are being 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

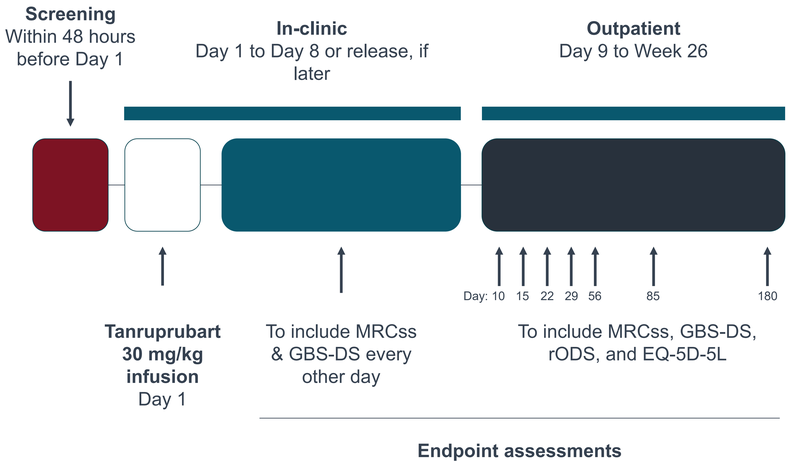
Study Design

- Patients who meet the eligibility criteria during screening are being enrolled to receive a single IV infusion of tanruprubart (30 mg/kg)
- Participants remain in the clinic for the completion of study assessments either until Day 8 or until they are cleared to be discharged, depending on which occurs later. Participants return for follow-up visits until the end of the study on Week 26 (**Figure 4**)
- The study is powered to compare MRCss at Week 1 with an IVIG-treated, external control group from the International GBS Outcome Study database[6]

Outcome Measures

- In addition to PK and PD analyses, the efficacy, safety and tolerability of tanruprubart are being assessed in this cohort
- Efficacy and participant quality of life are being assessed using the MRCss, GBS-DS scale, Rasch-built Overall Disability Scale (rODS), and EuroQol five-dimensional, five-level questionnaire (EQ-5D-5L)

Figure 4. GBS-FORWARD Study Design



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) is recruiting participants with recently diagnosed GBS in North America and Europe to confirm the generalizability of previous study findings
- This study will 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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Disclosures
GM, H-AK: Employees and shareholders of Annexon Biosciences. PL: Employee of Annexon Biosciences at the time of the study. JAA: Received honoraria, consultation fees, and served on advisory boards for Alexion, Alnylam, Akcea therapeutics, argenx SE, Annexon, Dianthus, CSL Behring, Hansa, Grifols, Immunovant, Immunopharm, ImmunoAbs, Sanofi, Johnson & Johnson, Pfizer, Takeda. SL, RM, KG: No relevant disclosures.
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