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Linking Early Complement Inhibition to Long-Term Outcomes in GBS: Objective Measures Support Tanruprubart Efficacy

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INTRODUCTION

- Guillain-Barré syndrome (GBS) is a rare, rapidly progressive neuromuscular emergency that can affect anyone at anytime, often requires prolonged hospitalization and intensive care, and in some cases can be fatal[1]
- Following exposure to an infectious agent, activation of C1q and the classical complement pathway by antibodies that cross-react with nerve components drives inflammation, motor neuron conduction block, nerve damage, and destruction that results in severe paralysis, morbidity, long-term disability, and in some cases, death[1-4]
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively binds to and inhibits C1q, the initiating molecule of the classical complement pathway, thus providing fast inhibition of complement-mediated neuroinflammation and nerve damage[5,6]
- GBS-02 (NCT04701164) was a Phase 3, multicenter, double-blind, placebo-controlled trial of tanruprubart in patients with GBS. The study met its primary endpoint demonstrating that patients treated with tanruprubart 30 mg/kg had a 2.41-fold higher likelihood of being in a better state of health relative to placebo at Week 8 on the GBS-disability scale (GBS-DS) score (GBS-DS odds ratio [OR] 2.4, 95% CI 1.3–4.5; p=0.0058). Consistent with the findings from the GBS-01 study, benefit observed with a higher dose of tanruprubart (75 mg/kg group) did not reach significance versus placebo at Week 8 (OR 1.2, 95% CI 0.65–2.2; p=0.5548)[7]
- Consistent benefit was observed across multiple secondary endpoints for tanruprubart 30 mg/kg, demonstrating clinically meaningful treatment benefit throughout the study[7]
- Tanruprubart was well tolerated, and most adverse events were mild to moderate in severity, attributed to GBS, and not considered related to study drug with the exception of rash. Rash was the most common infusion-related reaction; cases were mostly mild to moderate and resolved without sequalae[7]

OBJECTIVE

- To characterize early improvement in muscle strength, balance, coordination, and mobility in participants treated with tanruprubart 30 mg/kg and their impact on longer-term recovery

METHODS

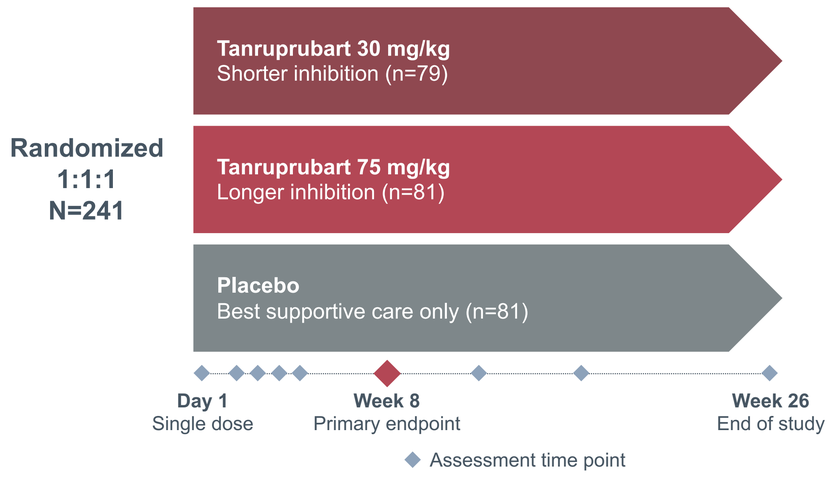
Outcomes

- Functional outcomes were analyzed up to Week 26 in the study:
  - Medical Research Council (MRC) sumscore, which evaluates muscle strength and is a prognostic factor for long-term outcomes.[8] The percentage of participants who could perform the Timed Up-and-Go (TUG) test and the standing heel-rise test (SHRT) were assessed using proportional odds
  - The percentage of participants who reached no limitations (score of 0) was analyzed on the Overall Neuropathy Limitations Scale (ONLS), which evaluates the severity of motor limitations,[9] and the GBS-DS, which measures overall disability, as well as the Rasch-built Overall Disability Scale (rODS; score of 48), which captures activity and social participation limitations[10]
  - This analysis was performed in the modified intent-to-treat analysis set (tanruprubart 30 mg/kg: n=79; placebo: n=81)

GBS-02 study design

Key inclusion/exclusion criteria:
- Aged ≥16 years
- With a GBS-DS 3, 4 or 5
- ≤10 days from onset of weakness
- Did not have access to intravenous immunoglobulin or plasma exchange
- Stratified by baseline prognostic factors: muscle strength and time from onset of weakness

Conducted at sites in Bangladesh and the Philippines



RESULTS

- Rapid and complete C1q inhibition was observed within 1 day of tanruprubart 30 mg/kg dosing with inhibition lasting approximately 1 week (**Figure 1**)
- Rapid and complete C1q inhibition was also achieved with tanruprubart 75 mg/kg, with a duration of inhibition of 2–3 weeks (**Figure 1**)
- Rapid improvements in muscle strength, mobility, balance, and coordination with tanruprubart 30 mg/kg versus placebo were observed as early as Week 1 and maintained through Week 26 (**Figures 2–4**)
- More participants treated with tanruprubart 30 mg/kg completely recovered on GBS-DS, reported no limitations on ONLS, and could easily perform all tasks on rODS=48 from Week 1 through Week 26 compared to placebo (**Figures 5–7**)

Figure 1. Tanruprubart and free C1q serum levels after treatment

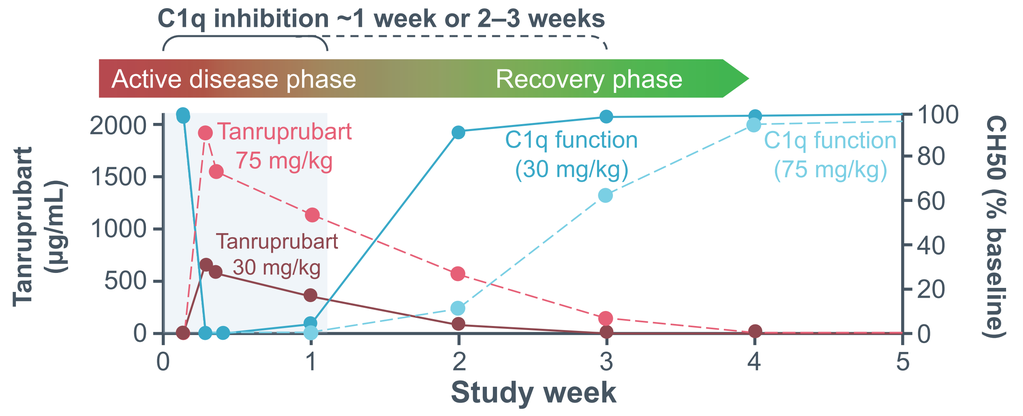


Figure 2. Change from baseline in MRC sumscore over time to Week 26

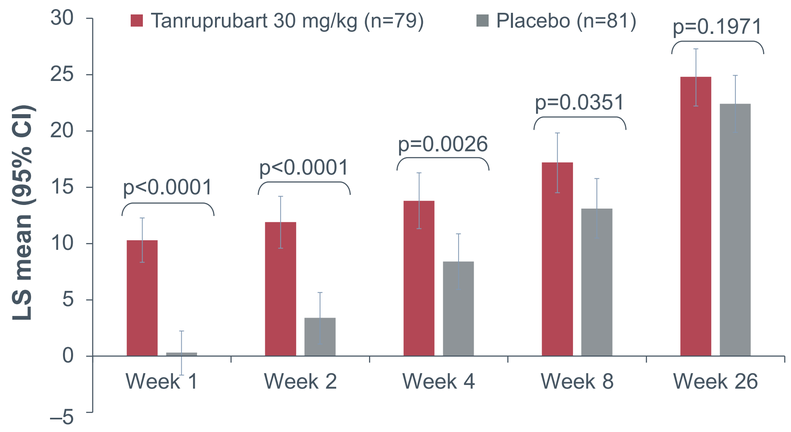


Figure 3. Proportion of patients able to perform TUG test over time to Week 26

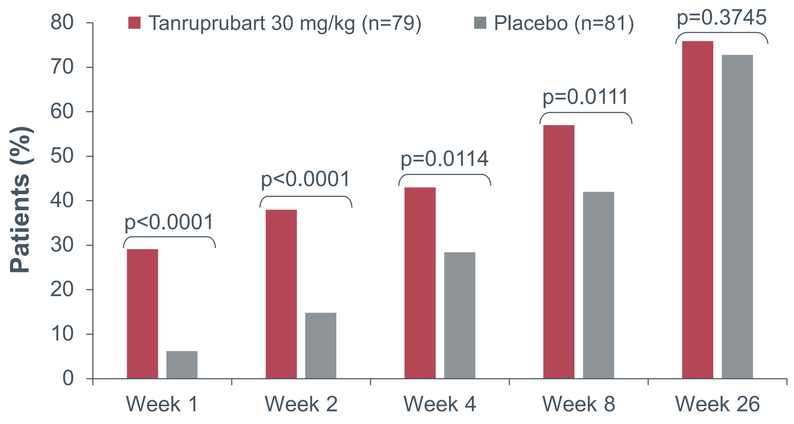


Figure 4. Proportion of patients able to perform SHRT assessments over time to Week 26

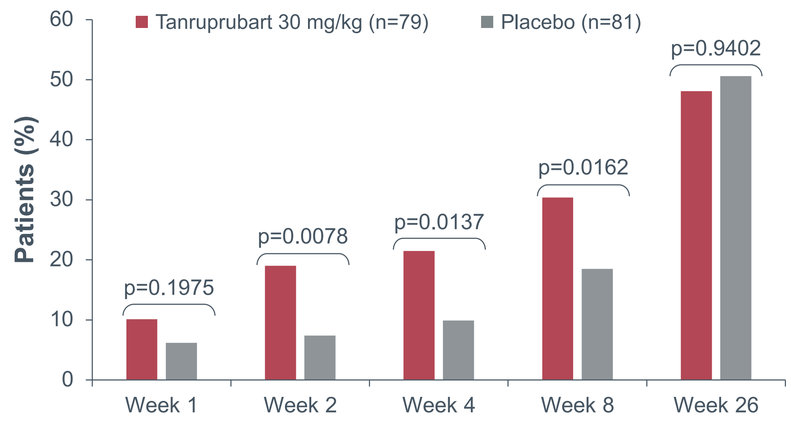


Figure 5. Proportion of patients who fully recovered (GBS-DS=0) over time to Week 26

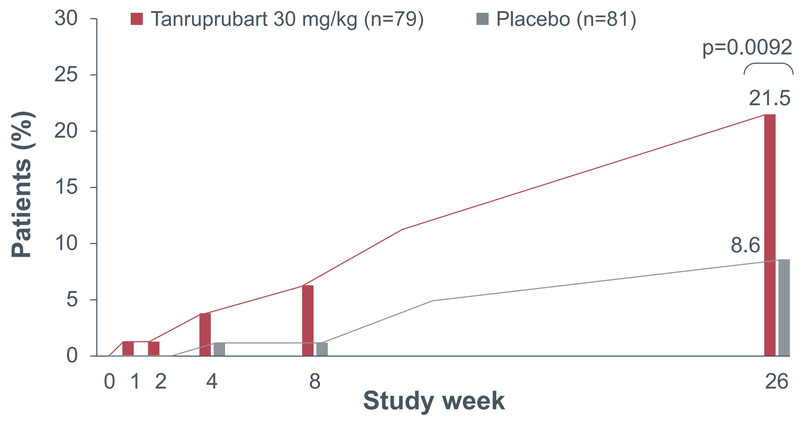


Figure 6. Proportion of patients reporting no limitations (ONLS=0) over time to Week 26

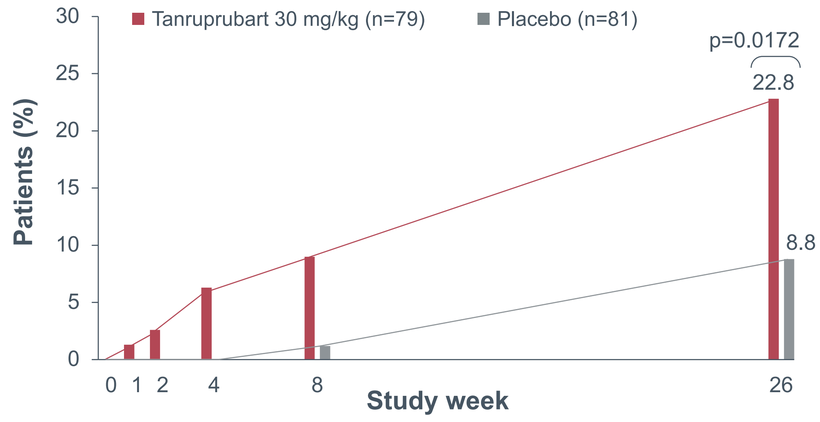
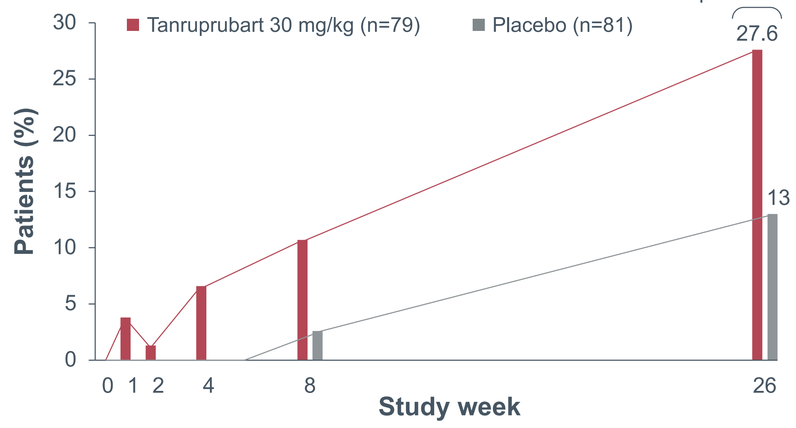


Figure 7. Proportion of patients reporting 'easy to perform' on all tasks (rODS=48) over time to Week 26



CONCLUSIONS

- **A single tanruprubart 30 mg/kg dose immediately and completely blocks C1q, shutting down the classical complement pathway, halting inflammation and nerve damage, and resulting in rapid clinical improvement in muscle strength as well as early clinically meaningful improvements in function, mobility, balance, and coordination**
- **Improvement in muscle strength is an early indicator of overall response in GBS,[8] and correlated with more participants who were able to fully recover across ONLS, GBS-DS, and rODS over the 26-week study period**
- **By reducing neuroinflammation and nerve damage, tanruprubart 30 mg/kg is a potential novel treatment which provides rapid and consistent clinically meaningful improvements in muscle strength and functional mobility for patients with GBS**

References

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