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Efficacy of Tanruprubart For the Treatment of Guillain-Barré Syndrome in a Broad Spectrum of Patients

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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]
- Multiple neurotypes of GBS have been identified in nerve conduction studies (NCS), and can depend on the NCS criteria used.[2,3] The relative frequencies of each NCS subtype vary across geographical regions[2]
- 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 rapid and complete inhibition of classical complement-mediated neuroinflammation and nerve damage[4,5]
- GBS-02 (NCT04701164) was a Phase 3, multicenter, double-blind, placebo-controlled trial of tanruprubart in patients with GBS that met the primary endpoint and demonstrated 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; odds ratio [OR] 2.4, 95% CI 1.3–4.5; p=0.0058). Consistent with 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)[6]
- GBS-02 primarily included the two most common NCS classifications of GBS: 61.9% with acute motor axonal neuropathy (AMAN) and 21.3% with acute inflammatory demyelinating polyneuropathy (AIDP), both of which involve the classical complement pathway[2,6]
  - Among patients in Europe and the USA in the International GBS Outcome Study (IGOS), ~60% had AIDP and ~80% had a Medical Research Council (MRC) sumscore >20; these patients tend to have relatively low serum neurofilament light (NfL) levels[7]
- Tanruprubart was well tolerated, and most adverse events were mild to moderate in severity, due to GBS, and not considered related to study drug. Rash was the most common infusion-related reaction; cases were mostly mild to moderate and resolved without sequalae[6]

OBJECTIVE

- To assess whether the findings of GBS-02 were applicable to a Western GBS population, this prespecified subgroup analysis compared the efficacy of tanruprubart 30 mg/kg in patients with moderate or severe GBS to subgroups that corresponded with Western disease characteristics

METHODS

Analysis populations

- The subgroups were defined by the following characteristics:
  - GBS classifications: AIDP or AMAN
  - Baseline MRC sumscore (muscle strength) >20 or ≤20, defined as a boundary for stratification in study GBS-02 based on a cluster analysis of data from IGOS Bangladesh-based GBS patients
  - Baseline serum NfL <353 pg/mL or ≥353 pg/mL; 353 pg/mL was the median baseline serum NfL level in the overall population

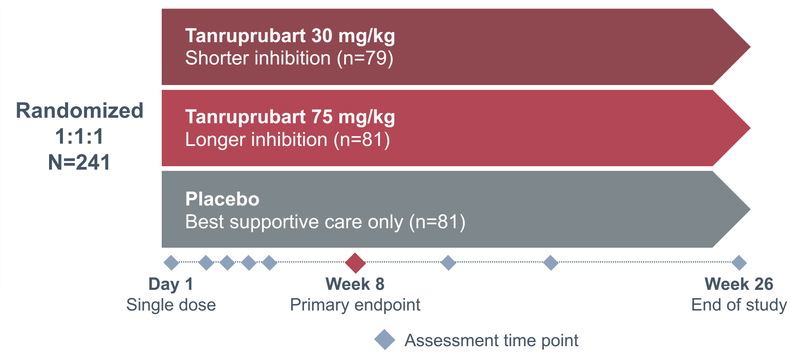
Assessments

- MRC sumscore at Week 1 and Week 8, and GBS-DS at Week 8 were assessed[8]
- Clinically meaningful outcomes, including Overall Neuropathy Limitations Scale (ONLS), ventilation duration, time to return to walking independently (GBS-DS ≤2), Timed Up-and-Go test scores and ventilation were also assessed overall and by GBS classifications
- All p values, with the exception of GBS-DS at Week 8 for the full analysis set, are nominal

GBS-02 study design

Patients included those:
- Aged ≥16 years
- With a GBS-DS 3, 4, or 5
- ≤10 days from onset of weakness
- Without 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

- GBS-DS and MRC sumscores were significantly improved through Week 8 with tanruprubart 30 mg/kg, irrespective of axonal (AMAN) or demyelinating (AIDP) NCS classification (**Table 1**)
  - Improvements in MRC sumscores were observed as early as Week 1
  - Improvements in ONLS, ventilation, and the time to walk independently were also observed
- Improvements in muscle strength and Timed Up-and-Go test scores were observed as early as Week 1 regardless of GBS NCS classification (**Figure 1**)
- Patients with AMAN and AIDP were 25 and 7 times more likely to return to normal (GBS-DS=0) with tanruprubart (30 mg/kg) treatment than with placebo, respectively (**Figure 2**)
- Consistently significant results were observed in the proportion of patients treated with tanruprubart 30 mg/kg who reached no limitations (ONLS=0) compared to placebo in both the AIDP and AMAN subgroups starting at Week 1 (**Figure 2**)
- Patients with milder disease (baseline MRC sumscore >20) experienced significant response compared to placebo across most measures, while those with MRC sumscore ≤20 had numerical improvement (**Table 1**)
- Patients with baseline serum NfL levels <353 pg/mL (milder disease) receiving tanruprubart 30 mg/kg generally reported significantly better outcomes compared to placebo than those with baseline NfL ≥353 pg/mL, although numerical improvement was still seen on most measures (**Table 1**)

Table 1. Primary and key secondary endpoints for the full analysis set and GBS classification subgroups with tanruprubart 30 mg/kg versus placebo

Primary	Endpoint	Assesses	Time point	Full analysis set (PBO n=81; Tanruprubart n=79)	AIDP (PBO n=18; Tanruprubart n=16)	AMAN (PBO n=49; Tanruprubart n=50)	MRC sumscore >20 (PBO n=49; Tanruprubart n=50)	MRC sumscore ≤20 (PBO n=38; Tanruprubart n=38)	Serum NfL <353 pg/mL (PBO n=40; Tanruprubart n=47)	Serum NfL ≥353 pg/mL (PBO n=39; Tanruprubart n=31)
1	GBS-DS: Odds ratio[a] (p value)	GBS disability	Week 8	**2.41 (0.0058)**	5.31 (0.0130)	**2.26 (0.0361)**	**3.03 (0.0102)**	1.51 (0.3651)	**2.65 (0.020)**	1.21 (0.688)
Secondary hierarchy	LS mean change[b] (p value)[c]									
2	ONLS	Functional disability	Week 8	−0.8 (0.0965)	−1.0 (0.3481)	−1.0 (0.1057)	**–2.5 (<0.0001)**	–0.4 (0.5410)	–1.2 (0.0674)	0.2 (0.8307)
3	MRC sumscore	Muscle strength	Week 8	**4.0 (0.0351)**	**9.4 (0.0259)**	4.0 (0.1022)	3.1 (0.2361)	4.9 (0.0772)	**5.4 (0.0324)**	1.6 (0.5561)
4	MRC sumscore	Muscle strength	Week 1	**10.0 (<0.0001)**	**11.9 (0.0002)**	**10.4 (<0.0001)**	**8.8 (<0.0001)**	**11.5 (<0.0001)**	**14.6 (<0.0001)**	3.7 (0.0711)
	Median fewer days (p value)[c]									
5	Ventilation[d]	Duration of ventilation – fewer days	Week 26	**28 days (0.0356)**	142 days p value N/A	14 days p value N/A	21.5 days p value N/A	29 days p value N/A	33 days (0.0909)	91.5 days (0.4679)
	Walking independently	Time to return to walking independently	Week 26	**31 days (0.0211)**	**41 days (0.0048)**	0 days (0.0902)	41 days (0.0943)	NC days (0.5161)	34 days (0.0800)	–13 days (0.9455)

[a]Odds ratio: Likelihood that a patient receiving tanruprubart is in a better state of health relative to placebo. [b]LS mean point improvement relative to placebo. [c]p values for nominal testing using two-sided α=0.05. [d]For those requiring ventilation. LS, least squares; N/A, not applicable; NC, not calculable; PBO, placebo.

Figure 1. MRC sumscore and Timed Up-and-Go test scores at Week 1 in GBS classification subgroups

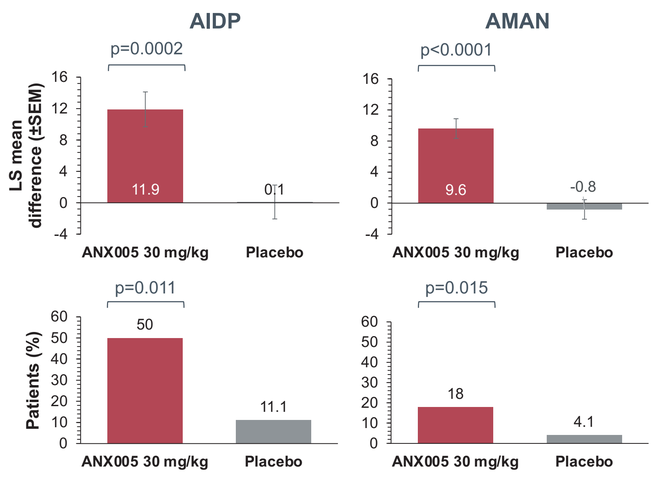
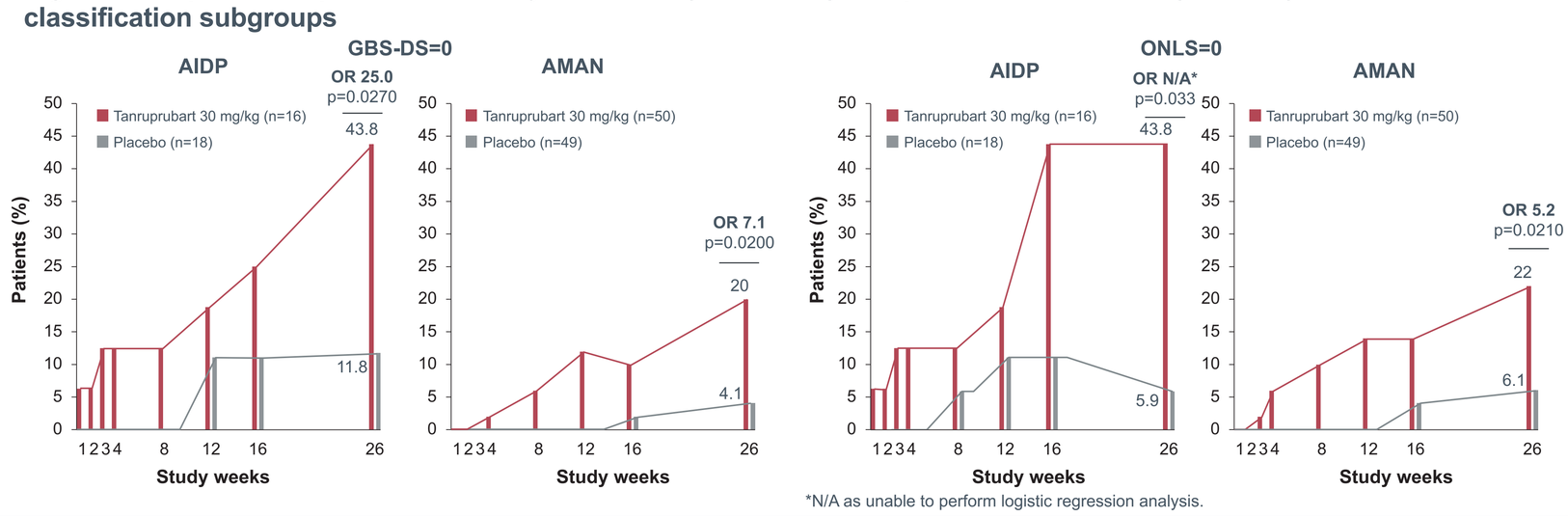


Figure 2. Proportion of patients who fully recovered (GBS-DS=0) or reported no limitations (ONLS=0) over time in GBS classification subgroups



*N/A as unable to perform logistic regression analysis.

CONCLUSIONS

- **Classical complement inhibition with a single dose of tanruprubart was associated with rapid and durable improvements in muscle strength, motor function, and overall health irrespective of GBS severity with deeper effects**
- **Patients with AMAN and AIDP were 25 and 7 times more likely to return to normal (GBS-DS=0) with tanruprubart (30 mg/kg) treatment than with placebo, respectively, with deeper treatment responses observed in the AIDP subgroup**
- **Tanruprubart was shown to be highly efficacious in patients with disease characteristics akin to US and European GBS populations reported in the IGOS cohort, supporting tanruprubart as a treatment for a broad spectrum of patients with GBS**

References:

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