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Targeted Immunotherapy With Tanruprubart (ANX005) Reduces Ventilation Requirements in Guillain-Barré Syndrome: A Phase 3 Subgroup Analysis

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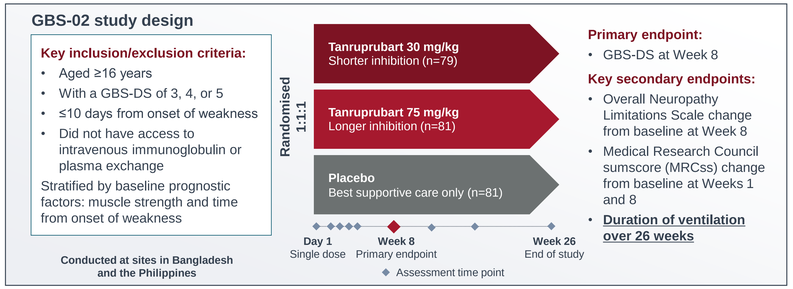
Introduction

- Guillain-Barré syndrome (GBS) is a rare, life-altering neuromuscular emergency requiring hospitalisation, and mechanical ventilation in severe cases[1]
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively inhibits 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]
- In GBS-02, a Phase 3, randomised, double-blind, placebo-controlled trial of tanruprubart 30 and 75 mg/kg (NCT04701164), a single infusion of tanruprubart 30 mg/kg led to early and sustained clinical benefit, and was well tolerated[4]
- This analysis evaluated the effect of tanruprubart 30 mg/kg on the duration of mechanical ventilation in GBS-02

Methods

- Participants aged ≥16 years with a recent GBS diagnosis and a GBS-disability score (GBS-DS) of 3 (able to walk 10 metres with help) to 5 (requiring ventilation) were randomised to receive a single intravenous dose of tanruprubart 30 or 75 mg/kg or placebo



Duration of ventilation analyses

- Ventilation day was any calendar day on which a participant received invasive mechanical ventilation for any duration; never-ventilated participants were assessed as 0 days
- Intubation and weaning were at the Principal Investigator's discretion
- The analysis population consisted of participants who required mechanical ventilation at any point after randomisation
- Ventilation duration was analysed using a zero-inflated negative binomial model to accommodate the excess of zeroes (participants who were never ventilated) and handle the overdispersion among those ventilated
- To avoid underestimation of ventilator burden for participants who died while on mechanical ventilation, they were assigned 182 days (the full trial length)
- Ventilation duration was assessed overall and by:
  - Muscle strength (MRCss; 0=tetraplegic, 60=normal), a stratification factor
  - Baseline GBS-DS
  - Axonal damage (neurofilament light [NfL] levels)

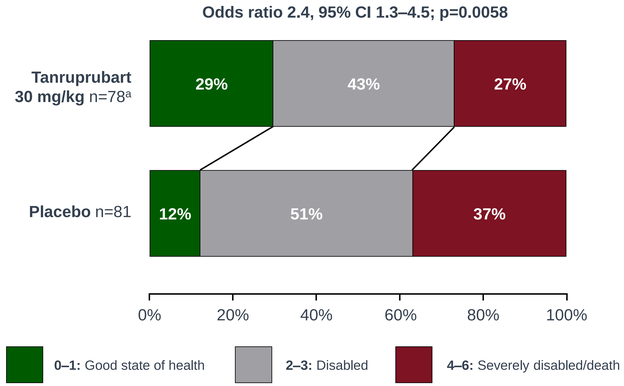
Results

- The 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-DS relative to placebo at Week 8 (**Figure 1**)

Ventilation outcomes

- Mechanical ventilation requirements were similar across treatment groups (**Table**)
  - Among ventilated patients, approximately 74% had a baseline GBS-DS of 5 (requiring assisted ventilation for at least part of the day)
- In the overall population, duration of ventilation was a median 28 days shorter with tanruprubart 30 mg/kg vs placebo (**Figure 2**)
- This difference was particularly notable in participants with the following baseline characteristics vs their healthier counterparts (**Figure 2**):
  - Greater muscle weakness (lowest baseline MRCss tertile 0–20): median 101 days shorter with tanruprubart 30 mg/kg vs placebo
  - Worse axonal damage (median baseline NfL ≥352.64): median 93 days shorter with tanruprubart 30 mg/kg vs placebo

Figure 1. GBS-02 primary endpoint: GBS-DS at Week 8



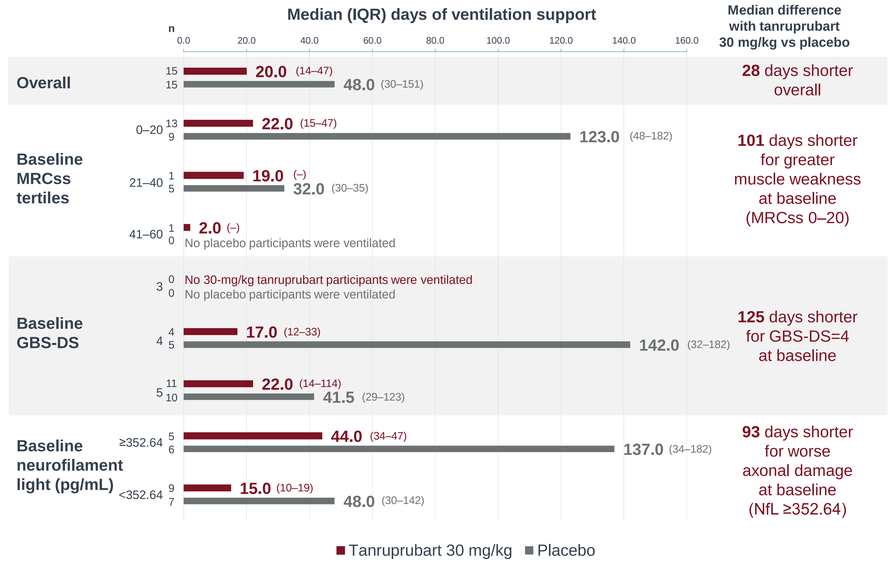
[a]1 patient in the tanruprubart 30 mg/kg group had missing data at Week 8.

Table. Number of mechanically ventilated participants overall and by baseline characteristics[a]

	Overall	Baseline MRCss			Baseline GBS-DS			Baseline NfL (pg/mL)	
Participants ventilated, n/N		**0–20**	**21–40**	**41–60**	**3**	**4**	**5**	**≥352.64**	**<352.64**
Tanruprubart 30 mg/kg (N=79)	15/79	13/38	1/37	1/4	0/12	4/56	11/11	5/31	9/47
Placebo (N=81)	15/81	9/38	5/35	0/7	0/7	5/64	10/10	6/39	7/40

[a]For patients who died while being mechanically ventilated, the duration of ventilation was imputed to 182 days (26 weeks).

Figure 2. Duration of mechanical ventilation with tanruprubart 30 mg/kg compared with placebo across baseline characteristics



IQR, interquartile range.

CONCLUSIONS

- Tanruprubart met the primary endpoint and significantly improved participants' state of health compared with placebo at Week 8
- Tanruprubart reduced the duration of mechanical ventilation in participants with GBS compared with placebo, especially among those with more severe disease
- Targeted classical complement inhibition with tanruprubart has the potential to improve critical clinical outcomes in GBS

References
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Conflicts of interest
H-AK, JD, RG, AN: Employment with and shareholder of Annexon Biosciences. QDM: Consultancy/advisory role with Annexon Biosciences. JN: Consultancy role with Annexon Biosciences. GM: Employee of Annexon Biosciences at the time of the study. KAKA: No relevant disclosures. ZI: Research funding from Fogarty International Center, National Institute of Neurological Disorders and Stroke of the National Institutes of Health, USA, and Annexon Biosciences. KCG: Consultancy/advisory role with Annexon Biosciences, argenx, Janssen, and Sanofi.
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