Targeted immunotherapy with Tanruprubart (ANX005) reduces ventilation requirements in Guillain-Barré syndrome (GBS)

Presenter: Henk-André Kroon, MD, MBA

Henk-André Kroon, MD, MBA[1]; Quazi Deen Mohammad, MBBS, MD, FCPS[2]; Jose Navarro, MD[3]; Glenn Morrison, MSc, PhD[1]; Ping Lin, MS[1]; Robert Gerwien, PhD[4]; Peter Collins[1]; Khan Abul Kalam Azad MBBS, FCPS, MD, FACP[5]; Zhahirul Islam, PhD[6]; Kenneth C. Gorson, MD[7]

[1]Annexon Biosciences, Brisbane, CA, USA; [2]National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [3]José R. Reyes Memorial Medical Center, Manila, Philippines; [4]Gerwien Analytical Solutions, Newington, CT, USA; [5]Dhaka Medical College and Hospital, Dhaka, Bangladesh; [6]Gut–Brain Axis Laboratory, icddr,b, Dhaka, Bangladesh; [7]St. Elizabeth's Medical Center, Boston, MA, USA

PRESENTED AT THE 11TH CONGRESS OF THE EUROPEAN ACADEMY OF NEUROLOGY | JUNE 21-24, 2025, HELSINKI, FINLAND

Acknowledgement: The study was sponsored by Annexon Biosciences (Brisbane, CA, USA). Medical writing and editing assistance were provided by Envision Pharma Group and were funded by Annexon Biosciences.

Tanruprubart (ANX005) is investigational and has not been approved for any indication in any jurisdiction

Conflicts of Interest

- **Henk-André Kroon:** Employee and shareholder of Annexon Biosciences
- **Quazi Deen Mohammad:** Consultancy/advisory role with Annexon Biosciences
- **Jose Navarro:** Consultancy/advisory role with Annexon Biosciences
- **Glenn Morrison:** Employee and shareholder of Annexon Biosciences
- **Ping Lin:** Employee and shareholder of Annexon Biosciences at the time of the study
- **Robert Gerwien:** Consultancy/advisory role with Annexon Biosciences
- **Peter Collins:** Employee and shareholder of Annexon Biosciences
- **Khan Abul Kalam Azad:** No disclosures
- **Zhahirul Islam:** Research funding from Fogarty International Center, National Institute of Neurological Disorders and Stroke of the National Institutes of Health, USA, and Annexon Biosciences
- **Kenneth C. Gorson**: Consultancy/advisory role with Annexon Biosciences, argenx, Janssen, and Sanofi

Neuromuscular respiratory failure common in GBS

Significant unmet need[1]

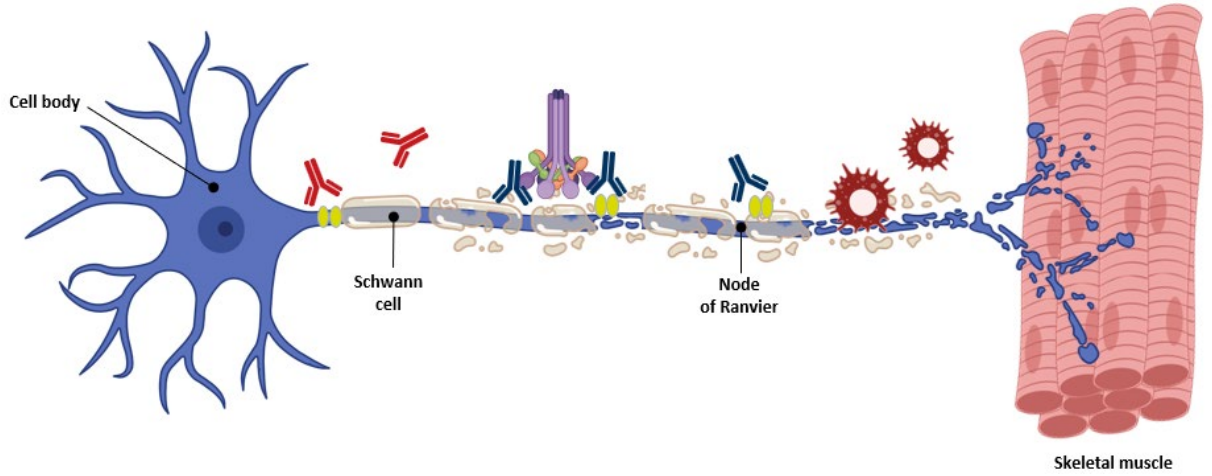
GBS is a rare, life-threatening post infectious neuromuscular emergency[2]

~7,000 people hospitalized and treated in the US per year[3] and **150,000** worldwide[1]

Despite current treatment:

~1 in 4 patients require mechanical ventilation[4,5]
Accounting for much of the global 1-year mortality rate[6] which ranges from **2–17%**

Antibody-mediated complement driven neuroinflammation and damage[1,7]

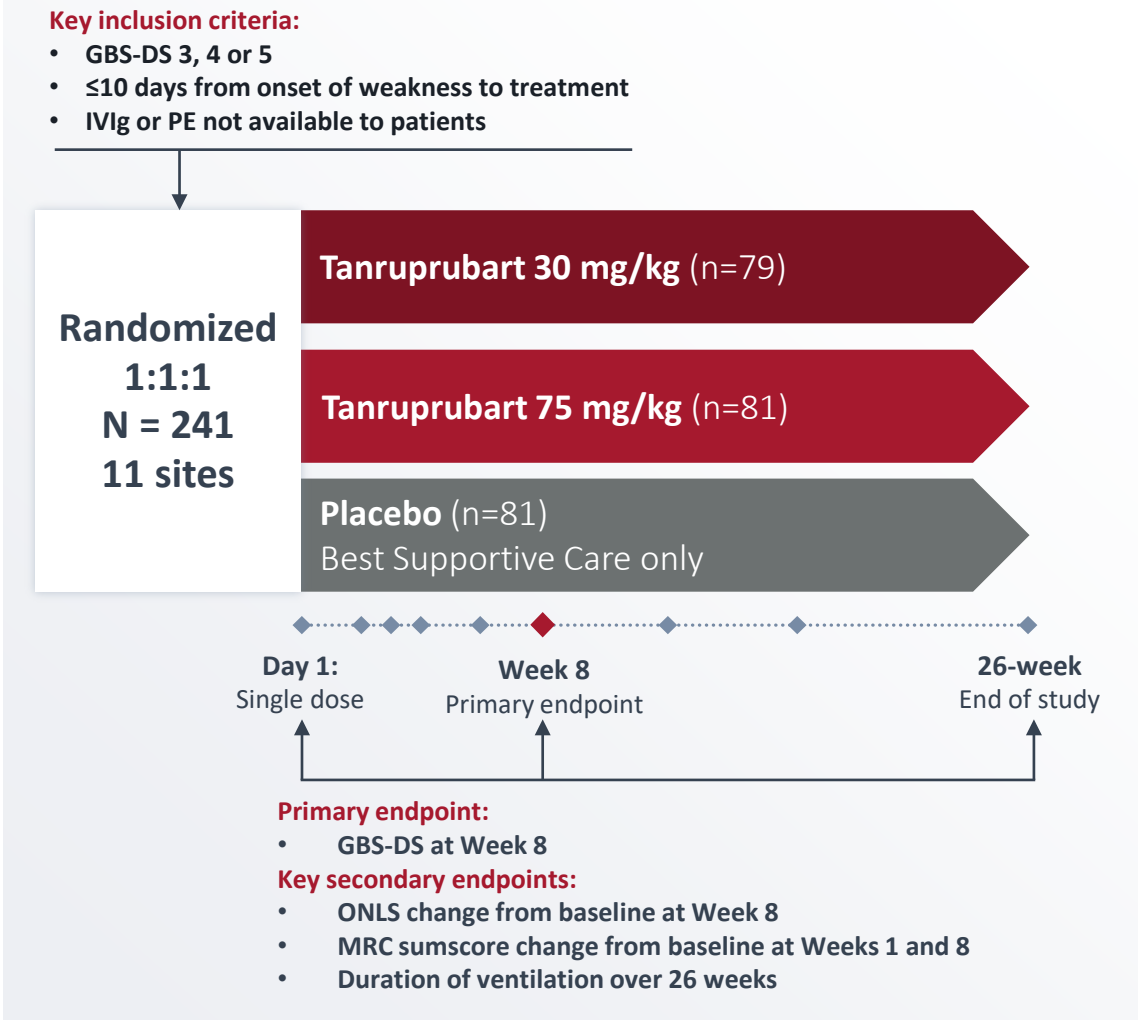


FDA, Food and Drug Administration; GBS, Guillain-Barré syndrome.

1. van Doorn PA. *Presse Med*. 2013;42(6 Pt 2):e193–201; 2. Willison HJ, et al. *Lancet*. 2016;388:717–27; 3. Annexon data on file; 4. Martic V, et al. *Can J Neurol Sci.* 2018;45:269–27; 5. van den Berg B, et al. *Nat Rev Neurol*. 2014;10:469–82; 6. Doets AY, et al. *Brain*. 2018;141:2866–77; 7. Dalakas MC, et al. *Nat Rev Neurol*. 2020;16:601–17.

A Phase 3, randomized, double-blind, placebo-controlled study of tanruprubart, an anti-C1q complement inhibitor

Well balanced across treatment groups



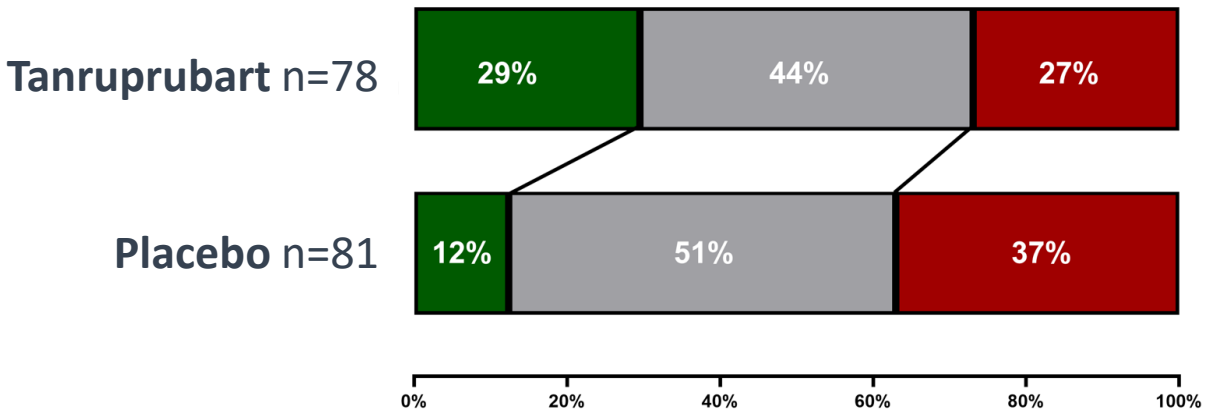
Baseline characteristic	Placebo (n=81)	Tanruprubart 30 mg/kg (n=79)	Tanruprubart 75 mg/kg (n=81)
Age, years, mean (SD)	34.2 (12.59)	36.9 (14.88)	37.9 (15.29)
Male sex, n (%)	57 (70.4)	51 (64.6)	51 (63.0)
Baseline GBS-DS, n (%)			
3	7 (8.6)	12 (15.2)	10 (12.3)
4	64 (79.0)	56 (70.9)	60 (74.1)
5	10 (12.3)	11 (13.9)	11 (13.6)
Baseline MRC sumscore, n (%)			
0–20	38 (46.9)	38 (48.1)	37 (45.7)
21–60	42 (51.9)	41 (51.9)	44 (54.3)
Time since onset of weakness to treatment, days, mean (SD)	6.5 (1.7)	6.3 (1.9)	6.6 (2.0)
Subtypes by Hadden criteria, n (%)			
AIDP	18 (22.2)	16 (20.3)	16 (19.8)
AMAN	49 (60.5)	50 (63.3)	50 (61.7)
Other	14 (17.3)	13 (16.5)	15 (18.5)

AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; GBS-DS, Guillain-Barré Syndrome Disability Score; IVIg, intravenous immunoglobulin; MRC, Medical Research Council; ONLS, Overall Neuropathy Limitations Scale; PE, plasma exchange; SD, standard deviation.

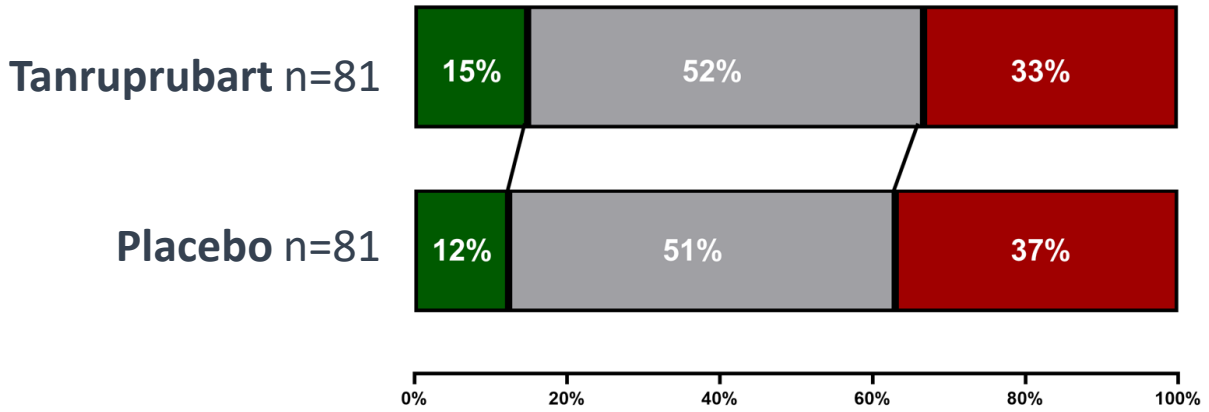
Tanruprubart 30 mg/kg met the primary endpoint

Tanruprubart 30 mg/kg treated participants were 2.4-fold higher likelihood of being in a better state of health relative to placebo

Tanruprubart 30 mg/kg
OR: 2.4 (95% CI 1.29–4.50), p=0.0058



Tanruprubart 75 mg/kg
OR: 1.2 (95% CI 0.65–2.22), p=0.5548



GBS-DS approach: Collapse 7-grade scale to a 3-grade scale (trichotomy)

0–1: Good state of health **2–3:** Disabled **4–6:** Severely disabled/death

CI, confidence interval; OR, odds ratio.

Tanruprubart was well tolerated, most adverse events were mild to moderate in severity, due to GBS, and were not considered related to the study drug

Majority of AEs were mild (Grade 1) to moderate (Grade 2)

- Most common related events were transient infusion-related reactions
- SAEs and Grade 3 AEs (including infections) were balanced across groups
- Pneumonias similar across groups and mostly associated with mechanical ventilation

Deaths

- No difference observed in incidence of all-cause mortality — 3 deaths in each dose group
  - Mortality rate of 3.7% consistent with rates seen in clinical trials

	Placebo n=81	Tanruprubart 30 mg/kg n=79	Tanruprubart 75 mg/kg n=81
	All Grades	All Grades	All Grades
Number of participants reporting TEAEs, n (%)	79 (97.5)	79 (100.0)	80 (98.8)
Number of participants with infusion-related reaction, n (%)	4 (4.9)	24 (30.4)	32 (39.5)
Rash (most common with IRR)	2 (2.5)	20 (25.3)	25 (30.9)
Most common TEAEs (non-IRR), n (%)			
Blood CPK increased	46 (56.8)	44 (55.7)	35 (43.2)
Musculoskeletal pain	35 (43.2)	36 (45.6)	26 (32.1)
ALT increased	23 (28.4)	21 (26.6)	23 (28.4)
Urinary tract infection	18 (22.2)	19 (24.1)	18 (22.2)
Hypokalemia	24 (29.6)	16 (20.3)	11 (13.6)
Constipation	10 (12.3)	15 (19.0)	17 (21.0)
AST increased	16 (19.8)	11(13.9)	17 (21.0)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatinine phosphokinase; IRR, infusion-related reaction; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Duration of ventilation analysis methodology

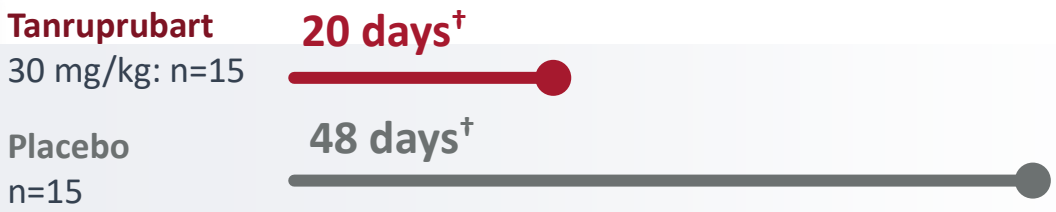
- Ventilation day definition: any calendar day on which a participant received invasive mechanical ventilation for any duration
  - Never ventilated were assessed as 0 days
- Intubation and weaning: timing and criteria at each Principal Investigator's discretion
- Analysis population: participants who required mechanical ventilation at any point after randomization
- Statistical model: ventilation duration was analysed using a zero-inflated negative binomial (ZINB) model to:
  - Accommodate the excess of zeroes (patients never ventilated)
  - Handle the overdispersion among those ventilated
- Imputation for death: to avoid underestimation of ventilator burden for participants who died while on mechanical ventilation they were assigned 182 days (the full trial length)
  - Seven out of nine deaths in study had been mechanically ventilated:
    - 3 Placebo
    - 2 Tanruprubart 30 mg/kg
    - 2 Tanruprubart 75 mg/kg
- Sensitivity analyses *(post-hoc):* Wilcoxon rank-sum test assessed the impact of the imputation strategy and baseline characteristics on reported duration of ventilation

Tanruprubart 30 mg/kg meaningfully reduces ventilation compared to placebo across multiple analyses

Seven out of nine deaths in study had been mechanically ventilated

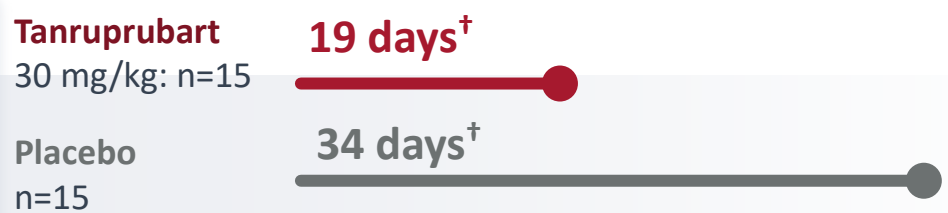
Imputed*

OFF VENTILATION EARLIER
28 days earlier, p=0.0356‡



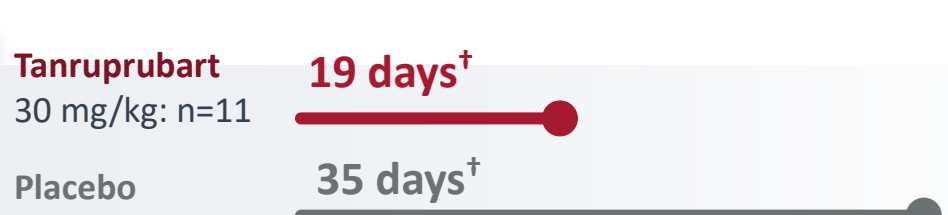
Non-Imputed

OFF VENTILATION EARLIER
15 days earlier, p=0.0079§



Ventilated At First Dose

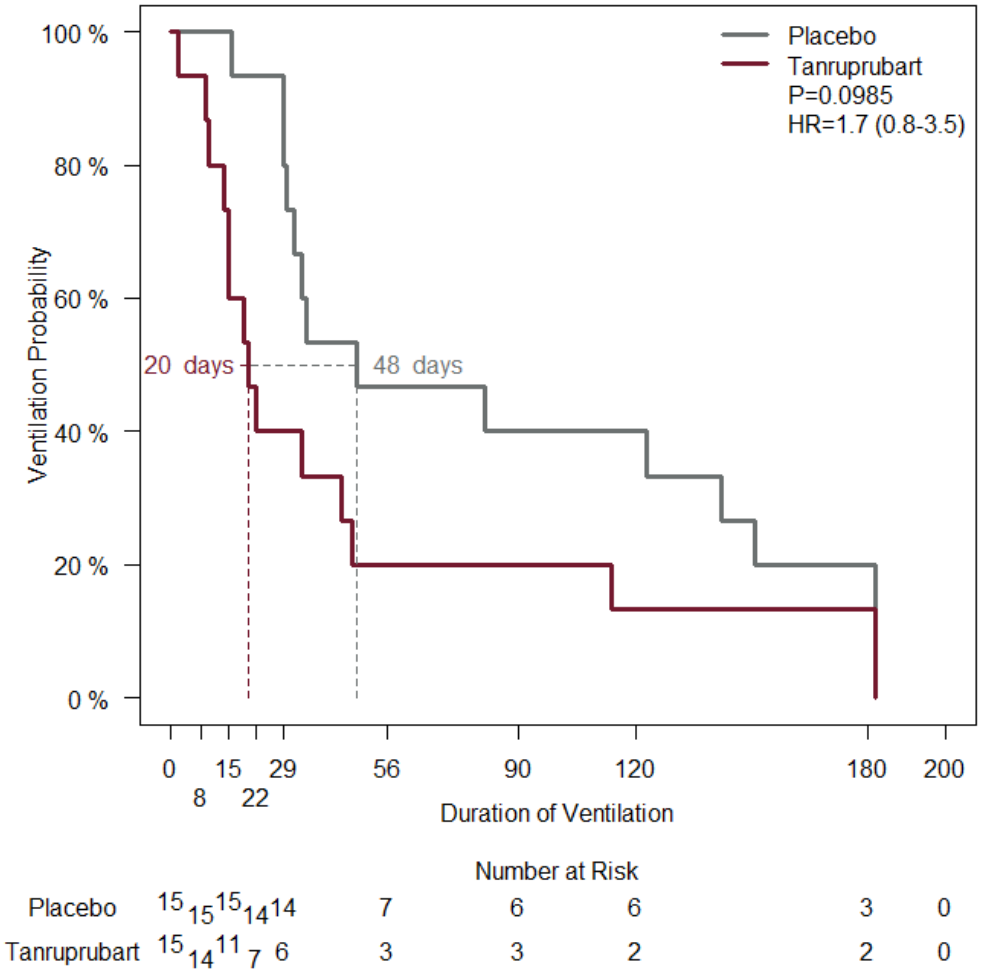
OFF VENTILATION EARLIER
16 days earlier, p=0.0137§



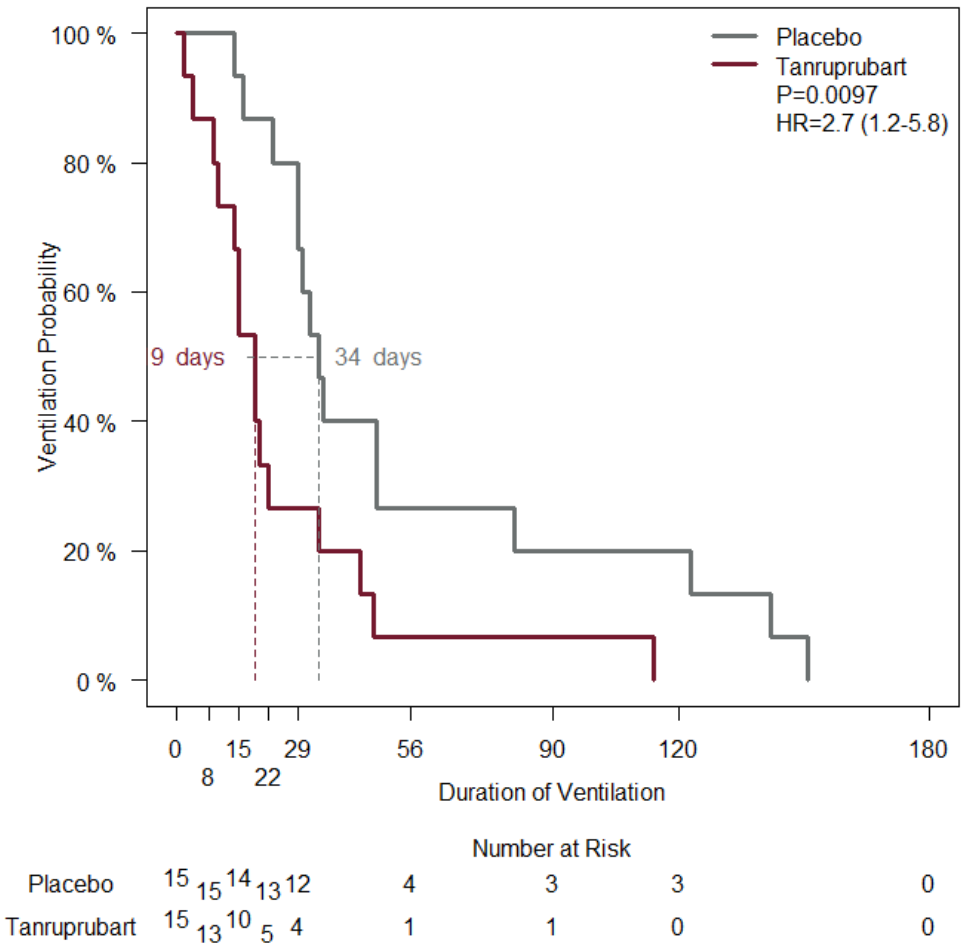
*Participants who died and required mechanical ventilation were imputed with 182 days (full duration); †Median; ‡Nominal, analyzed via ZINB; §Nominal, analyzed via Wilcoxon Rank Sum Test
‡Including one patient who was ventilated after GBS-DS baseline assessment but before receiving their first dose

Tanruprubart 30 mg/kg consistently reduced duration of ventilation compared to placebo

Imputed*



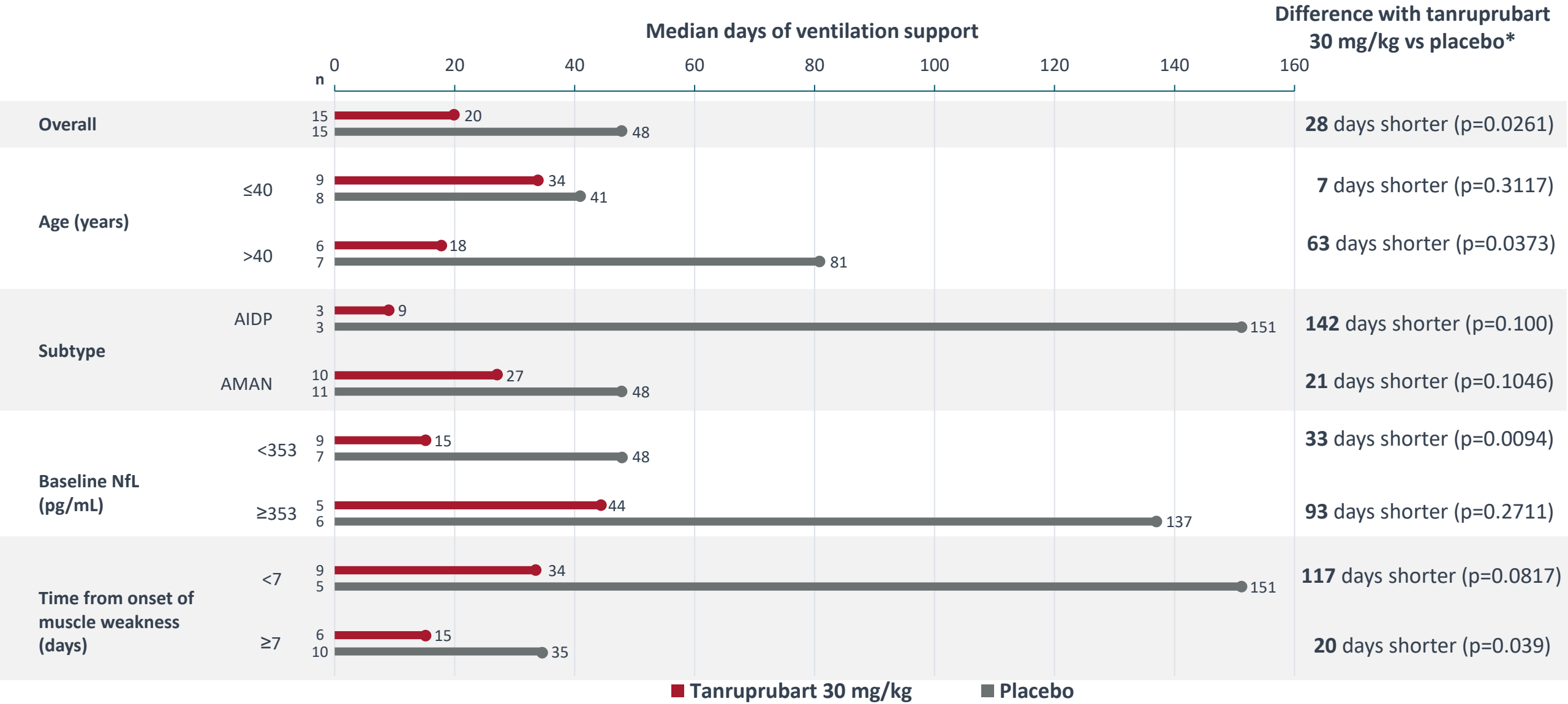
Non-Imputed



-------Time until 50% of patients are off ventilation

*Participants who died while requiring mechanical ventilation were imputed with 182 days (full duration).

Consistent benefit on ventilation across subgroups with tanruprubart 30 mg/kg



*Nominal; participants who died and required mechanical ventilation were imputed with 182 days (full duration); analyzed via Wilcoxon Rank Sum Test

Conclusion

- Tanruprubart 30 mg/kg met the primary endpoint of GBS-DS at Week 8 and resulted in a reduction in ventilator dependence versus placebo
- Tanruprubart was generally well tolerated
- Outcomes of ventilation duration consistent across analytical methods and subgroups
- Tanruprubart is a targeted immunotherapy with the potential to improve critical clinical outcomes in GBS