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Targeted Immunotherapy With Tanruprubart Reduces Ventilation Requirements in Guillain-Barré Syndrome (GBS)

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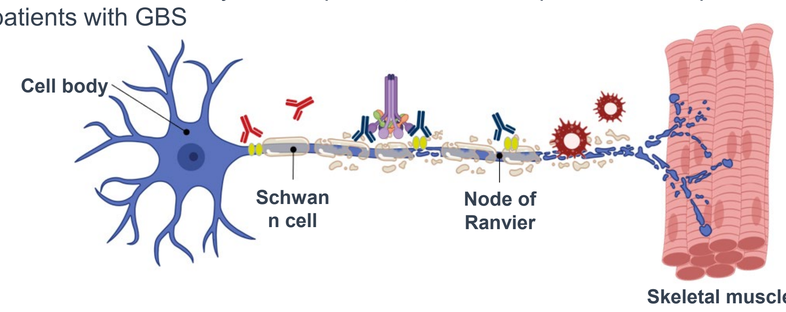
INTRODUCTION

- Guillain-Barré syndrome (GBS) is a rare, life-threatening, post infectious neuromuscular emergency that represents a significant unmet need[1,2]: ~7,000 people in the US per year[3] – and 150,000 people worldwide[1] – are hospitalized and treated for GBS
- Despite current treatment, the global one-year mortality rate ranges from 2–17%,[4] with an increased mortality rate of up to 20%[5,6] observed in the ~one in four patients requiring mechanical ventilation[1,7,8]
- GBS is characterized by antibody-mediated, classical complement-driven neuroinflammation with motor nerve conduction block, nerve damage, and nerve destruction[9]
- GBS-02 (NCT04701164) was a Phase 3, randomized, double-blind, placebo-controlled study of tanruprubart, an anti-C1q classical complement inhibitor, in patients with GBS



OBJECTIVE

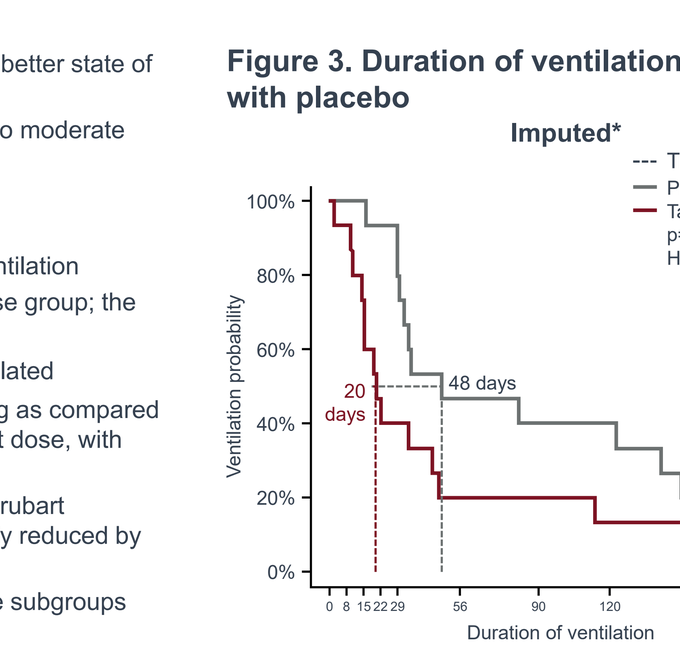
- To evaluate the impact of tanruprubart on duration of ventilation, a critical disease burden marker, in GBS-02

METHODS

GBS-02 study design

Key inclusion criteria:

- **GBS-disability score (GBS-DS) 3, 4, or 5**
- **≤10 days from onset of weakness to treatment**
- **Intravenous immunoglobulin or plasma exchange not available to patients**



Primary endpoint:

- **GBS-DS at Week 8**

Key secondary endpoints:

- **Overall Neuropathy Limitations Scale change from baseline at Week 8**
- **Medical Research Council (MRC) sumscore change from baseline at Weeks 1 and 8**
- **Duration of ventilation over 26 weeks**

Duration of ventilation analyses

- Ventilation day definition: 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: 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 analyzed using a zero-inflated negative binomial (ZINB) model to:
  - Accommodate the excess of zeroes (participants 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 occurred in participants who 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

RESULTS

- Tanruprubart 30 mg/kg, but not 75 mg/kg, significantly increased the likelihood of being in a better state of health by 2.4-fold relative to placebo at Week 8 (**Figure 1**)
- Tanruprubart was generally well tolerated; most adverse events (AEs) were mild (Grade 1) to moderate (Grade 2) and not considered related to the study drug
  - The most common drug-related events were transient infusion-related reactions
  - Serious AEs and Grade 3 AEs (including infections) were balanced across groups
  - Pneumonia cases were similar across groups and mostly associated with mechanical ventilation
  - No difference was observed in incidence of all-cause mortality – three deaths in each dose group; the mortality rate (3.7%) was consistent with rates seen in other clinical trials
  - Seven out of nine deaths in the study were participants who had been mechanically ventilated
- A significant reduction in the duration of ventilation was observed with tanruprubart 30 mg/kg as compared with placebo across multiple analyses, including imputed, not imputed, and ventilated at first dose, with participants taken off ventilation up to 28 days earlier compared with placebo (**Figure 2**)
- Duration of ventilation over time was significantly reduced in participants treated with tanruprubart 30 mg/kg compared with placebo (not imputed), while duration of ventilation was significantly reduced by 28 days in the imputed group (**Figure 3**)
- The median number of days on ventilation support was consistently reduced across multiple subgroups with tanruprubart 30 mg/kg compared with placebo (**Figure 4**)

Figure 1. GBS-DS scores with tanruprubart 30 mg/kg and 75 mg/kg at Week 8 (primary endpoint)

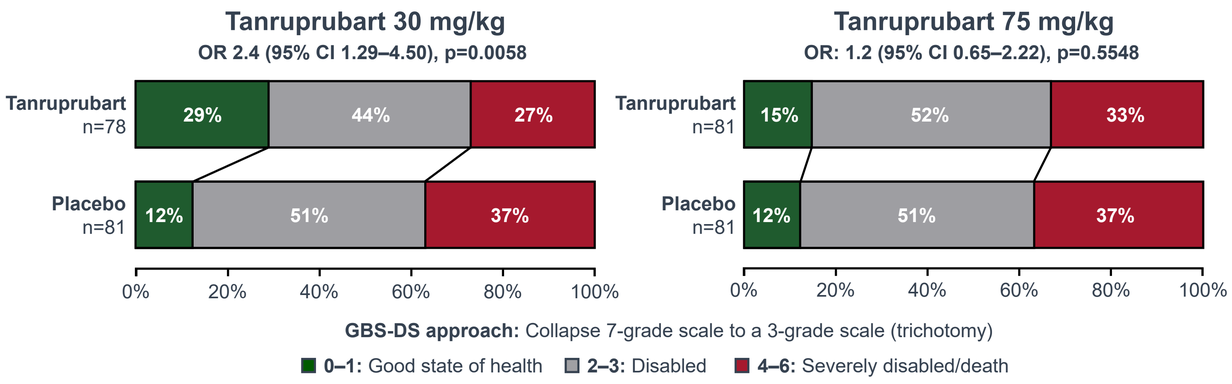
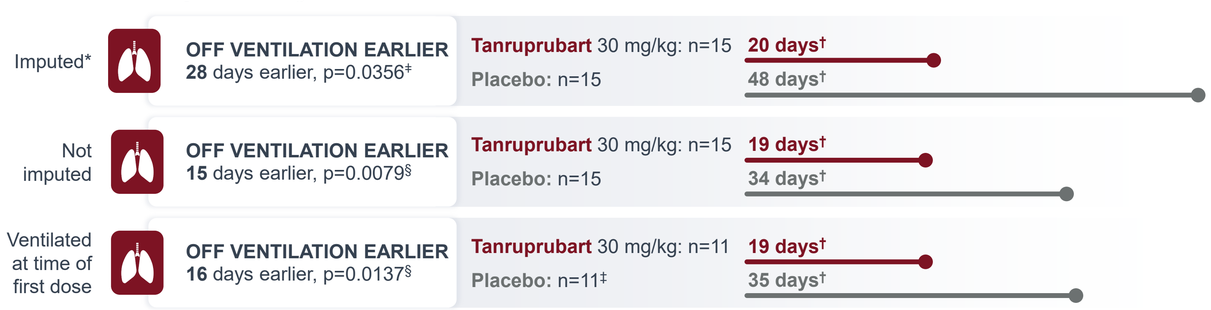


Figure 2. Duration of ventilation with tanruprubart 30 mg/kg compared with placebo across multiple analyses

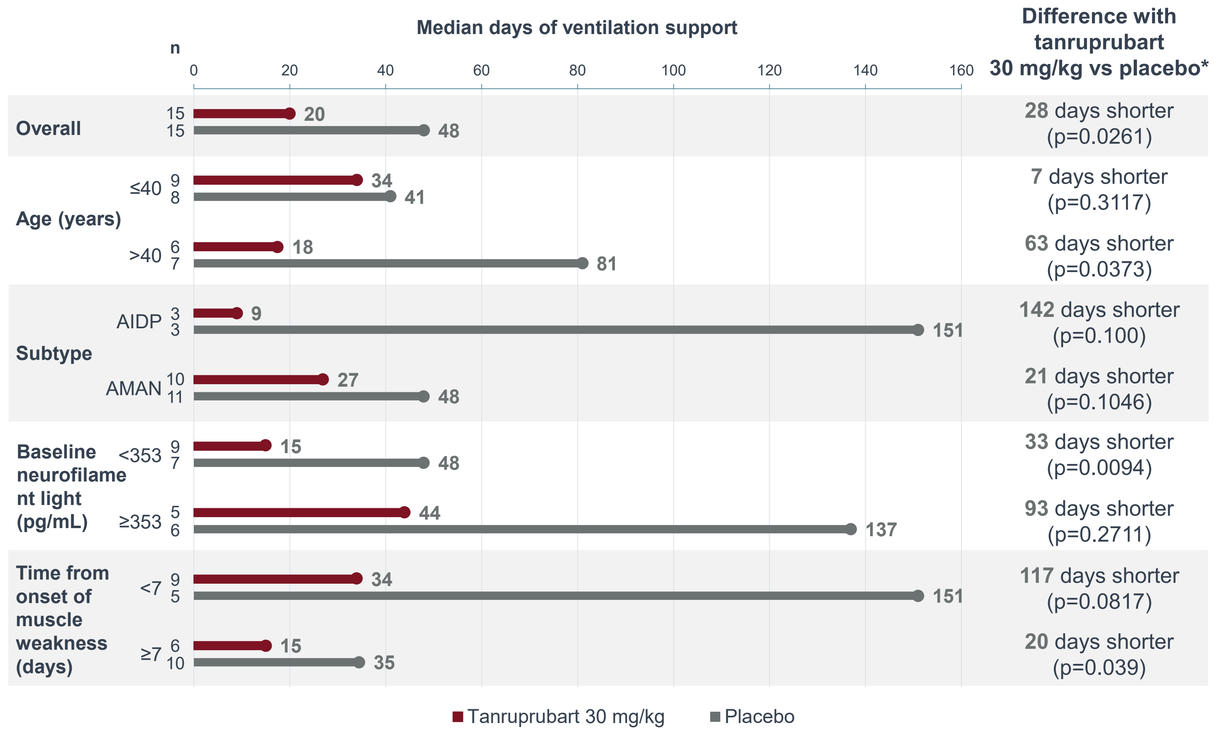


*Participants who died and required mechanical ventilation were imputed with 182 days (full duration); †Median; ‡Nominal, analyzed via ZINB; §Nominal, analyzed via Wilcoxon rank-sum test ‡Including one patient who was ventilated after GBS-DS baseline assessment but before receiving their first dose

Figure 3. Duration of ventilation over time with tanruprubart 30 mg/kg compared with placebo

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

Figure 4. Duration of ventilation with tanruprubart 30 mg/kg compared with placebo across observed subgroups



*Nominal; participants who died and required mechanical ventilation were imputed with 182 days (full duration); analyzed via Wilcoxon rank-sum test

CONCLUSIONS

- **Tanruprubart met the primary endpoint and significantly improved participant's state of health compared with placebo at Week 8**
- **Tanruprubart was generally well tolerated and did not result in an increase of infections, despite not requiring vaccination or antibiotic prophylaxis**
- **Participants treated with tanruprubart had a significant reduction in duration of ventilation compared with placebo, which was consistent across multiple analyses and patient types**
- **Targeted classical complement inhibition with tanruprubart has the potential to improve critical clinical outcomes in GBS**

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Disclosures

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