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A Novel Guillain-Barré Syndrome Clinical Progression Scale to Characterise the Patient's Care Journey: Utilisation in a Phase 3 Trial of Tanruprubart

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Introduction

- Guillain-Barré syndrome (GBS) is a rare, acute, life-altering autoimmune polyneuropathy that is characterised by rapidly progressive weakness and prolonged recovery[1]
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively inhibits C1q, the initiating molecule of the classical complement pathway, enabling rapid and complete inhibition of classical complement-mediated neuroinflammation and nerve damage[2,3]
- GBS-02 (NCT04701164) was a Phase 3, multicentre, randomised, double-blind, placebo-controlled study of tanruprubart in patients with GBS (N=241) in Bangladesh and the Philippines[4]
- We describe a novel GBS Clinical Progression Scale (CLIPS) used in GBS-02 to characterise the patient's care trajectory during the acute and recovery phases of GBS

Methods: CLIPS development

- CLIPS was developed to describe the care trajectory of patients with GBS by capturing transitions across levels of care over time
- The CLIPS was adapted by the study sponsors and GBS experts, based on the World Health Organization (WHO) COVID-19 Clinical Progression Scale,[5] which is an ordinal measure based on levels of care (**Table 1**), and designed to be globally applicable and healthcare system–agnostic
- The CLIPS scale is an 8-grade ordinal measure classifying the level of GBS-specific management and supportive care required, rather than functional status (**Table 2**)
- In GBS-02 the CLIPS was administered by the physician weekly for 4 weeks, and then at 2, 3, 4, and 6 months, providing a cumulative insight into the level and duration of care provided during the 26-week study period (**Figure 1**)

Table 1. WHO Clinical Progression Scale[5]

Patient state	Descriptor	Score
Uninfected	Uninfected: no viral RNA detected	0
Ambulatory mild disease	Asymptomatic; viral RNA detected	1
	Symptomatic; independent	2
	Symptomatic; assistance needed	3
Hospitalised: moderate disease	Hospitalised; no oxygen therapy[a]	4
	Hospitalised; oxygen by mask or nasal prongs	5
Hospitalised: severe disease	Hospitalised; oxygen by NIV or high flow	6
	Intubation and mechanical ventilation, pO_2/FiO_2 ≥150, or SpO_2/FiO_2 ≥200	7
	Mechanical ventilation, pO_2/FiO_2 <150 (SpO_2/FiO_2 <200), or vasopressors	8
	Mechanical ventilation, pO_2/FiO_2 <150, and vasopressors, dialysis, or ECMO	9
Dead	Dead	10

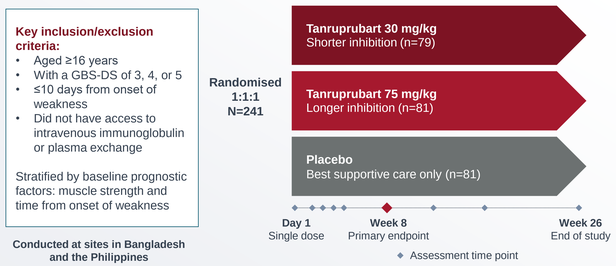
[a]If hospitalised for isolation only, record status as for ambulatory patient.
ECMO, extracorporeal membrane oxygenation; FiO_2, fraction of inspired oxygen; NIV, non-invasive ventilation; pO_2, partial pressure of oxygen; SpO_2, oxygen saturation.

Table 2. GBS Clinical Progression Scale (CLIPS)[a]

Grade	Description of the Grade
0	Discharged home, independent ADL, capable of self-care
1	Requiring ongoing nursing care or assistance by trained caregivers in ADL
2	Requiring intensive physical/occupational/speech therapy and/or general medical or nursing care during recovery
3	Hospitalised, requiring ongoing medical or nursing care during GBS progression or recovery
4	Not mechanically ventilated but requiring intensive monitoring
5	Receiving non-invasive ventilation or high-flow oxygen
6	Receiving invasive mechanical ventilation
7	Death

[a]CLIPS is a novel scale that is not validated and is not intended to predict or assess treatment effect or make treatment decisions.
ADL, activities of daily living.

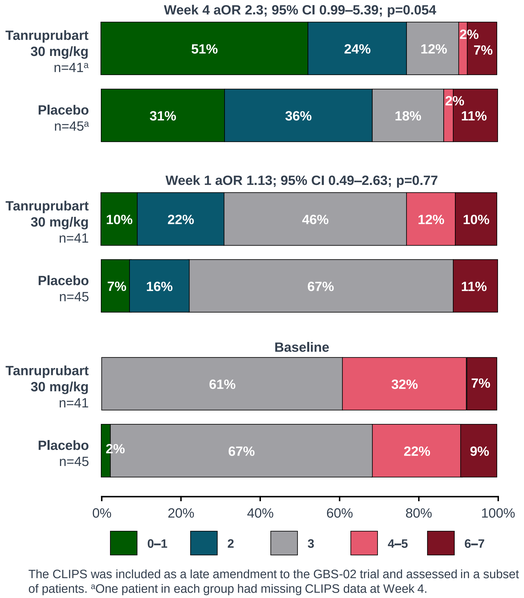
Figure 1. GBS-02 study design



Results: CLIPS outcomes

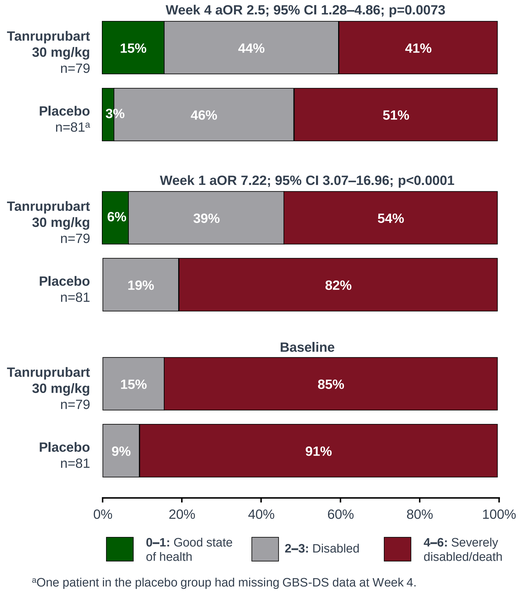
- All patients were hospitalised and most required medical intervention at baseline (Grade ≥3; **Figure 2**)
- By Week 1, care requirements decreased (**Figure 2**)
- In a prespecified analysis at Week 4, the odds of requiring less care favoured tanruprubart 30 mg/kg over placebo on the CLIPS (adjusted odds ratio [aOR] 2.3; 95% CI 0.99–5.39; p=0.054; **Figure 2**)
- These results were consistent with functional outcomes used to establish treatment effect (Week 4 aOR 2.5; 95% CI 1.28–4.86; p=0.0073; **Figure 3**)
- The CLIPS provided a practical insight into the level of care and supportive measures required by patients with GBS
- To our knowledge, CLIPS is the first GBS-specific tool designed to map the patient care trajectory by grading the level of care and supportive management required over time, rather than functional status alone

Figure 2. CLIPS at baseline, Week 1, and Week 4



The CLIPS was included as a late amendment to the GBS-02 trial and assessed in a subset of patients. [a]One patient in each group had missing CLIPS data at Week 4.

Figure 3. GBS-DS at baseline, Week 1, and Week 4



[a]One patient in the placebo group had missing GBS-DS data at Week 4.

CONCLUSION

- CLIPS offers a pragmatic, healthcare system–agnostic lens on the GBS care journey, enabling cross-country comparison of acute disease burden and supportive care needs
- Early separation on CLIPS at Week 4 favouring tanruprubart 30 mg/kg vs placebo supports a clinically meaningful shift toward lower resource intensity during early GBS
- These findings support the promising potential of tanruprubart in treating patients with GBS

References
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Conflicts of interest
H-AK, PP: Employment with and shareholder of Annexon Biosciences. KCG: Consultancy/advisory role with Annexon Biosciences, argenx, Janssen, and Sanofi. QDM: Consultancy/advisory role with Annexon Biosciences. TH: Consultancy/advisory role with Dianthus Therapeutics, Sanofi, Janssen, Nuvig, Biocryst, argenx, AbbVie, Amgen, and Annexon Biosciences.
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