ID #1196

Early Muscle Strength Improvements in Participants With GBS Treated With Tanruprubart Is a Predictor of Better Outcomes

Glenn Morrison[1], Henk-André Kroon[1], Zhahirul Islam[2], Kenneth C. Gorson[3], Khan Abul Kalam Azad[4], Jose Navarro[5], Peter Collins[1], Quazi Deen Mohammad[6]

[1]Annexon Biosciences, Brisbane, CA, USA; [2]Gut-Brain Axis Laboratory, icddr,b, Dhaka, Bangladesh; [3]St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA, USA; [4]Dhaka Medical College and Hospital, Dhaka, Bangladesh; [5]José R. Reyes Memorial Medical Center, Manila, Philippines; [6]National Institute of Neuroscience (NINS), Dhaka, Bangladesh

INTRODUCTION

- Guillain-Barré syndrome (GBS) is a rare, complement-mediated peripheral neuropathy characterized by rapidly progressive muscle weakness[1,2]
- Following exposure to an infectious agent, antibodies that cross-react with nerve components activate C1q and the classical complement pathway driving neuroinflammation and nerve damage with motor neuron conduction block, severe paralysis, long-term disability, and in some cases, death[1-4]
- Muscle strength, measured by Medical Research Council sumscore (MRCss) is one of the strongest predictors of GBS prognosis and a core component of prognostic tools, including the modified Erasmus GBS Outcome Score (mEGOS)[5]
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively inhibits C1q, providing rapid inhibition of classical complement-mediated neuroinflammation and nerve damage[6,7]
- GBS-02 (NCT04701164) was a Phase 3, multicenter, double-blind, placebo-controlled study of tanruprubart in patients with GBS.
  - Participants treated with a single dose of tanruprubart 30 mg/kg were significantly more likely to achieve a better state of health by Week 8, assessed by the GBS-Disability Scale (GBS-DS) than those receiving placebo[8]
- Participants enrolled had mean (SD) baseline MRCss of 21.8 (13.54) and 21.1 (11.87) in the placebo and tanruprubart 30 mg/kg groups, respectively
- Tanruprubart 30 mg/kg–treated participants demonstrated more than a 10-point improvement in MRCss compared to placebo, with 87% of participants treated with tanruprubart 30 mg/kg showing improvement from baseline, versus 46% with placebo (p<0.0001)
- Tanruprubart was generally well tolerated, and most adverse events were mild to moderate in severity

OBJECTIVE

- To evaluate the correlation of muscle strength at Week 1 with subsequent disability, functional mobility, and quality of life outcomes in GBS-02 up to Week 26

METHODS

Outcomes

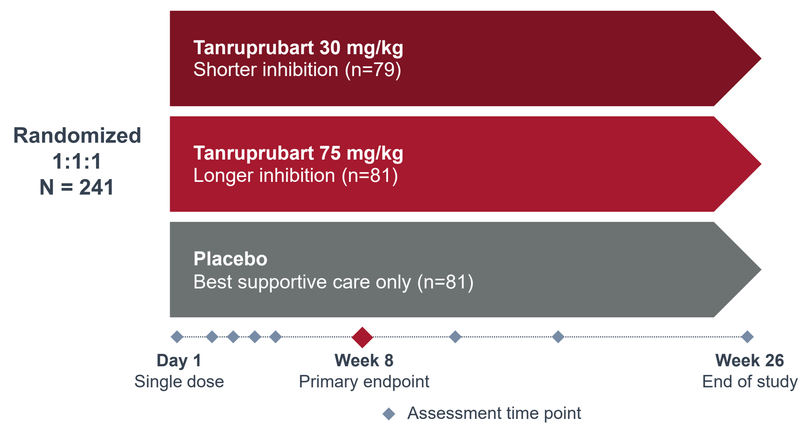
- MRCss at Week 1, analyzed using least square (LS) means, was a key secondary outcome in GBS-02
- In addition, the following outcomes were analyzed up to Week 26:
  - Disability outcomes: GBS-DS to assess overall disability and Overall Neuropathy Limitations Scale (ONLS) to assess motor limitation severity[9]
  - Functional mobility outcomes: Rasch-built Overall Disability Scale (r-ODS)[10] and the Timed Up-and-Go (TUG) test
- Correlation analysis
  - Correlations between MRCss at Week 1 and the above outcomes were assessed in the pooled study population using Kendall's tau estimates and Pearson's correlation coefficient

GBS-02 study design

Key inclusion/exclusion criteria:
- Aged ≥16 years
- With a GBS-DS of 3, 4, or 5
- ≤10 days from onset of weakness
- Did not have 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

Effect of tanruprubart on muscle strength

- Tanruprubart 30 mg/kg and 75 mg/kg led to rapid improvements in muscle strength by Week 1, with MRCss LS mean differences of 10.0 and 8.3 points vs placebo, respectively (p<0.0001)
  - MRCss improvement at Week 1 versus baseline was achieved by 87.0% and 95.1% of participants receiving tanruprubart 30 mg/kg and 75 mg/kg, respectively, compared with 45.7% receiving placebo

Correlation between muscle strength at Week 1 and disability (pooled population, n=160)

- Higher MRCss at Week 1, indicating greater muscle strength, were significantly correlated with durable improvements in overall disability and motor limitations over time (**Table**, **Figure 1** and **Figure 2**)
- Higher MRCss at Week 1 were also correlated with participants achieving the milestones of running and returning to normal functionality (**Table**)

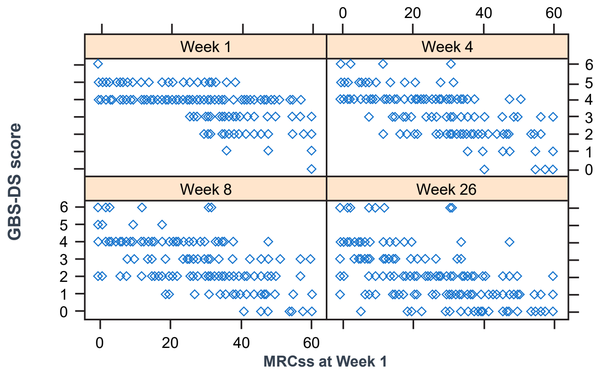
Correlation between muscle strength at Week 1 and functional mobility (pooled population)

- Significant correlations were observed between higher MRCss at Week 1 and durable improvements over time in functional mobility outcomes, including r-ODS scores which assess activity and social participation limitations (**Figure 3**)
- Durable improvements over time in the TUG test were also significantly correlated with MRCss at Week 1, indicating a consistent predictive effect (**Figure 4**)

Table. Correlations between MRCss at Week 1 and disability outcomes

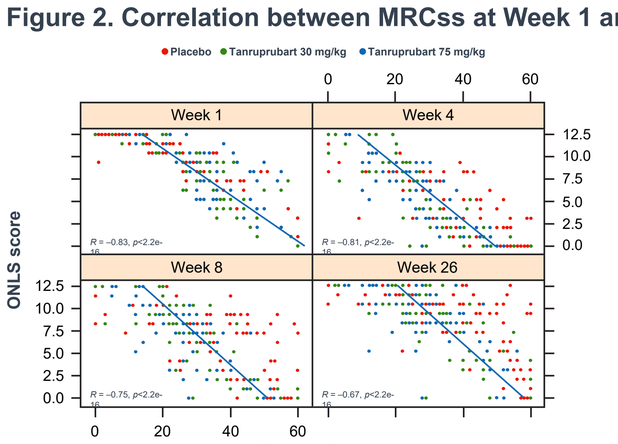
Correlation vs GBS-DS			Correlation vs ONLS total score		
GBS-DS milestone at Week 26	**Pearson r**	**p value**	**ONLS milestone**	**Pearson r**	**p value**
Score of 0 (return to normal)	0.38	<0.0001	Score of 0 (return to normal) at Week 26	0.41	<0.0001
Score of ≤1 (able to run)	0.53	<0.0001	Time to 1-point improvement	–0.54	<0.0001

Figure 1. Correlation between MRCss at Week 1 and GBS-DS score over time



Correlation vs GBS-DS		
Week	**Tau**	**p value**
1	–0.51	<0.0001
4	–0.60	<0.0001
8	–0.55	<0.0001
26	–0.55	<0.0001

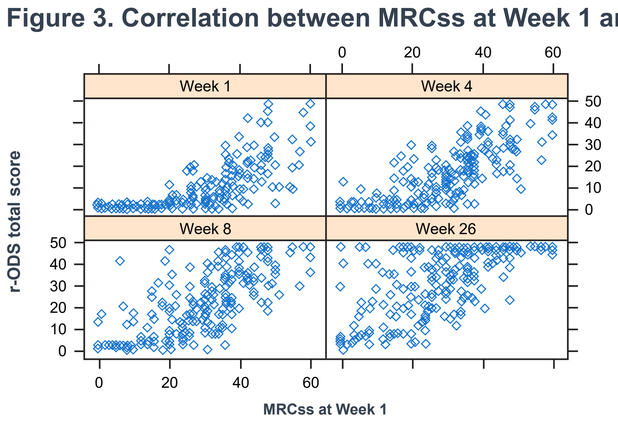
Figure 2. Correlation between MRCss at Week 1 and ONLS total score* over time



*Decreasing ONLS scores indicate improvement.

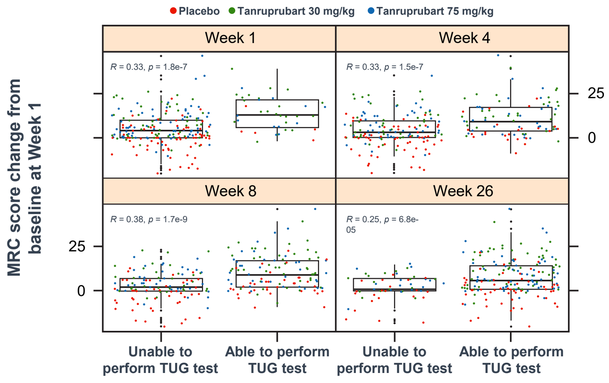
Correlation vs ONLS total score		
Week	**Tau**	**p value**
1	–0.73	<0.0001
4	–0.67	<0.0001
8	–0.59	<0.0001
26	–0.52	<0.0001

Figure 3. Correlation between MRCss at Week 1 and non-transformed r-ODS total score over time



Correlation vs non-transformed r-ODS total score		
Week	**Tau**	**p value**
1	0.65	<0.0001
4	0.62	<0.0001
8	0.59	<0.0001
26	0.50	<0.0001

Figure 4*. Correlation between MRCss at Week 1 and ability to perform TUG test over time



*Box plots show the median (bold horizontal line), interquartile range (rectangle), and range (whisker) MRCss at Week 1.

Correlation vs ability to perform TUG test		
Week	**r**	**p value**
1	0.33	<0.0001
4	0.33	<0.0001
8	0.38	<0.0001
26	0.25	<0.0001

CONCLUSIONS

- **Week 1 muscle strength (MRCss) strongly correlated with durable improvements in long-term disability and mobility outcomes across the 26-week study, confirming its value in prognostic tools like mEGOS**
- **MRCss was significantly improved with tanruprubart 30 mg/kg at Week 1 compared to placebo, which translated to improvement across the 26-Week study**
- **Rapid gains in muscle strength with tanruprubart likely reflect reduced complement-mediated inflammation and edema, allowing early restoration of nerve conduction in intact motor neurons and limiting ongoing nerve damage for early and sustained functional benefit**

References

1. Willison HJ, et al. *Lancet*. 2016;388:717–27. 2. van den Berg B, et al. *Nat Rev Neurol*. 2014;10:469–82. 3. Van Doorn PA. *Presse Med*. 2013;42:e193–201. 4. McGonigal R, et al. *Acta Neuropathol Commun*. 2016;4:23. 5. Walgaard C, et al. *Neurology*. 2011;76:968–75. 6. Lansita JA, et al. *Int J Toxicol*. 2017;36:449–62. 7. Suri P, et al. *Neurology*. 2022;98(18 Suppl):3867. 8. Kroon H-A, et al. Poster presented at the Neuromuscular Study Group Annual Scientific Meeting, 20–22 September 2022, Tarrytown, NY, USA. 9. Graham RC, Hughes RAC. *J Neurol Neurosurg Psychiatry*. 2006;77:973–6. 10. van Nes SI, et al. *Neurology*. 2011;76:337–45.

Acknowledgments

The study was sponsored by Annexon Biosciences (Brisbane, CA, USA). Medical writing and editing assistance were provided by Envision Ignite, an Envision Medical Communications agency, a part of Envision Pharma Group and were funded by Annexon Biosciences.

Disclosures

GM, H-AK, PC: Employment with and shareholder of Annexon Biosciences. 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. KAKA: No relevant disclosures. JN: Consultancy role with Annexon Biosciences. QDM: Consultancy/advisory role with Annexon Biosciences.

For additional information, please reach out to Glenn Morrison: gmorrison@annexonbio.com.

Presented at the 26th Neuromuscular Study Group Scientific Meeting, September 26–28, 2025; Stresa, Italy