# Comparative Efficacy: ANX005's Potential Advantage Over Intravenous Immunoglobulin in Guillain-Barré Syndrome

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**Henk-André Kroon, MD, MBA[1]; Kunal Kanani, PharmD, MBA[1]; Eric Humphriss, MBA[1]; Preeti Paliwal, PhD[1]; Benjamin Hoehn, MD, PhD[1]; AJ Acker[1]; Christos Stylianou, PhD[2]; Zhahirul Islam, PhD[3]; Nowshin Papri, MBBS, MPH[3]; Quazi Deen Mohammad, MD[4]**

[1]Annexon Biosciences, Brisbane, CA, US; [2]ClinBAY, Limassol, Cyprus; [3]Laboratory of Gut Brain Axis, Infectious Diseases Division, icddr,b, Dhaka, Bangladesh; [4]National Institute of Neuroscience (NINS), Dhaka, Bangladesh

## INTRODUCTION

- Guillain-Barré syndrome (GBS) is an acute inflammatory disease characterized by rapid antibody-mediated injury of the peripheral nervous system following infection[1-3]
- Despite treatment with intravenous immunoglobulin (IVIg), the current standard of care, approximately 25% of patients demonstrate progressive muscle weakness.[2] Mortality rates range from 3%-10%.[4]
- Approximately 25% of patients with GBS require mechanical ventilation, which leads to poor functional outcomes and increases in mortality risk[3]
- In GBS, antibodies targeting specific pathogens cross-react with the peripheral nervous system, causing activation of the classical complement pathway[5]
- ANX005 is a monoclonal antibody that inhibits C1q, the initiating molecule of the classical complement pathway in blood and cerebrospinal fluid, and provides early inhibition of complement-mediated neural damage[6,7]
- Results from a randomized placebo-controlled phase 1b study (GBS-01) of patients with GBS receiving ANX005 indicate that an early increase in muscle strength influences long-term functional outcomes[8]
- An indirect comparison was completed to evaluate and compare the efficacy of ANX005 to that of IVIg from historical datasets of studies in patients with GBS

## METHODS

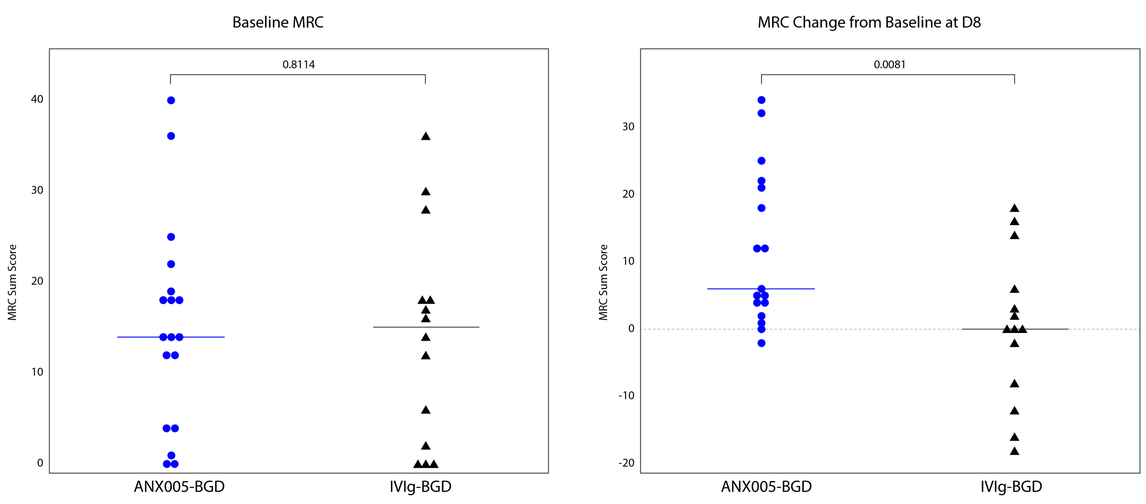
- Efficacy in GBS patients receiving a single ANX005 dose (18, 36, and 75 mg/kg) in the GBS-01 study in Bangladesh (BGD) was evaluated via indirect treatment comparison with patients who received IVIg in a prospective non-interventional study in BGD or patients with poor prognosis in the Second IVIg Dose (SID-GBS) study conducted in the Netherlands[9-11]
- Patients were matched for age, GBS-Disability Score (GBS-DS), and muscle strength by Medical Research Council (MRC) sum score
- Muscle strength assessed by MRC sum score (range 0-60) was analyzed using an independent sample t-test
- GBS-DS was analyzed using a proportional odds logistic regression model at Week 4 or 8

## RESULTS

### GBS-01 and BGD Cohort Comparison

- A total of 18 patients receiving ANX005 18-75 mg/kg in GBS-01 were compared to 14 patients receiving IVIg
- All patients had a baseline MRC sum score <40
- At baseline, there was no significant difference in mean MRC sum score between patients receiving ANX005 and IVIg (p=0.8114, **Figure 1A**)
- By Week 1, mean change from baseline in MRC sum score (range) for patients receiving ANX005 was 6 (-2 to 34) compared to 0 (-18 to 18) in patients receiving IVIg (p=0.0081, **Figure 1B**)

**Figure 1. MRC Sum Score in Patients Receiving ANX005 and IVIg at A) Baseline and B) Week 1**



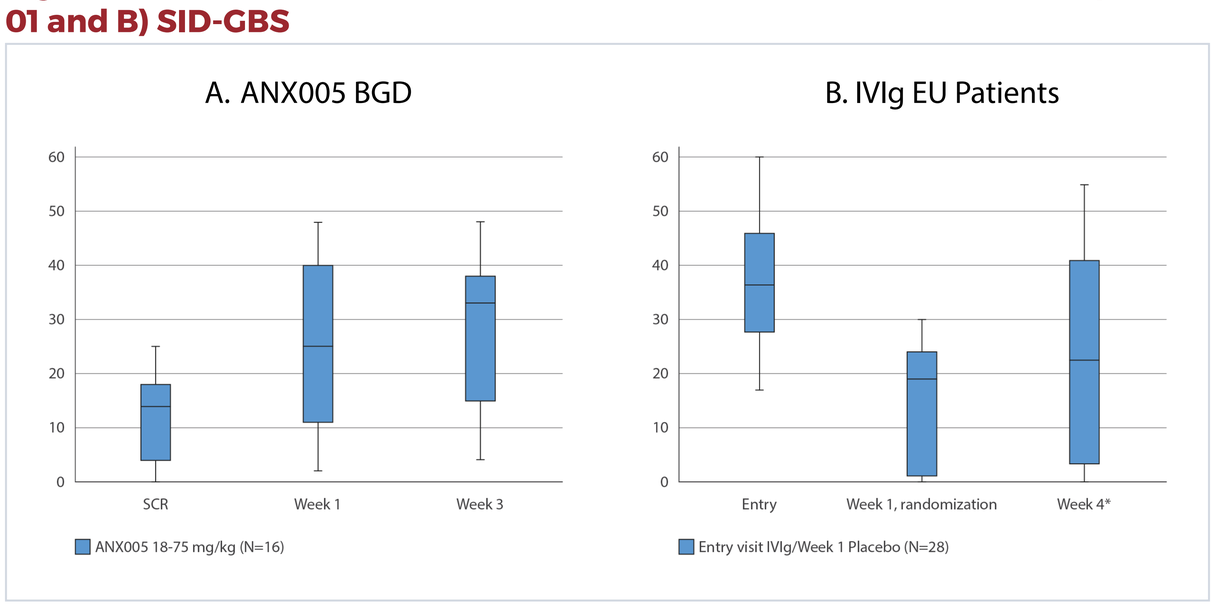

For baseline MRC sum score, n=18 for the ANX005 BGD Cohort and n=14 for the IVIg BGD Cohort.
*One patient receiving ANX005 had a missing MRC value at Week 1, therefore, only 13 patients treated with IVIg were used for comparison of change from baseline in MRC sum score.
BGD, Bangladesh; IVIg, intravenous immunoglobulin; MRC, Medical Research Council.

- At Week 1, 88% (15/17) of patients showed an improvement in muscle strength from baseline with ANX005 compared to 46% (6/13) of patients treated with IVIg
- The benefit of improvement in muscle strength at Week 1 with ANX005 translated at Week 4 into an odds ratio for improvement in GBS-DS of 2.50 (95%CI: 0.625, 10.007; p=0.1949) adjusted for baseline GBS-DS

### GBS-01 and SID-GBS Comparison

- The treatment effect in patients treated with ANX005 (n=16) was compared to GBS patients with poor prognosis (baseline MRC sum score 0-30) from the SID-GBS study who received placebo after a single 5-day course of IVIg (n=28)[9]
- Baseline median MRC sum score in GBS-01 on the day of ANX005 administration was 14 (IQR, 4-18), which was comparable to the baseline median MRC sum score of 19 (IQR, 12-35) in patients receiving IVIg; baseline was defined as immediately after a 5-day course of IVIg
- Three weeks after treatment completion, patients administered a single dose of 18-75 mg/kg ANX005 showed improved median MRC sum score of 33 (**Figure 2A**) compared to a score of 23 for patients receiving placebo after 5 days of IVIg in the SID-GBS trial (**Figure 2B**)

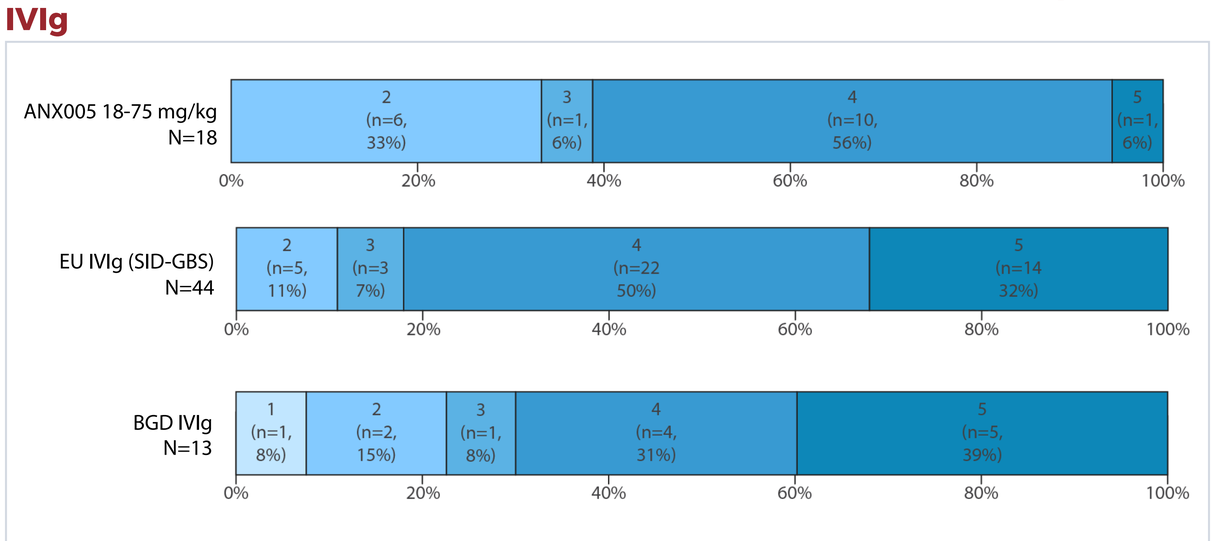
**Figure 2. Median MRC Sum Score at Baseline and Weeks 1 and 3 for A) GBS-01 and B) SID-GBS**




*Comparison of MRC sum score utilized outcomes at Week 3 for GBS-01 (3 weeks after randomization at Week 0) and Week 4 for SID-GBS patients (3 weeks after randomization at Week 1).
BGD, Bangladesh; EU, European Union; GBS, Guillain-Barré syndrome; IVIg, intravenous immunoglobulin; MRC, Medical Research Council; SCR, screening; SID, Second IVIg Dose.

- Among patients receiving ANX005, 5.6% required mechanical ventilation (GBS-DS=5) compared to 32% of patients on IVIg in the SID-GBS study (p=0.0247), consistently showing the benefit in patients receiving ANX005 compared to both patient populations (**Figure 3**)

**Figure 3. GBS-DS at Week 4 in Patients Treated with ANX005 Compared to IVIg**




BGD, Bangladesh; GBS, Guillain-Barré syndrome; IVIg, intravenous immunogobulin; SID, Second IVIg Dose.

## CONCLUSION

- Patients from BGD receiving ANX005 demonstrated early improvement in MRC sum score compared to patients receiving IVIg with comparable GBS severity from BGD and the Netherlands
- There was a shift to better health status in both comparisons, with mechanical ventilation required by fewer patients receiving ANX005 than patients receiving IVIg
- These results indicate that the early improvement in MRC sum score exhibited by patients receiving ANX005 compared to standard of care may translate to improved functional outcomes and possibly reduced ventilation time

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## DISCLOSURES

**HAK, KK, EH, PP, BH, AJA:** Employment with Annexon Biosciences; equity ownership in Annexon Biosciences.
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**QDM:** Consultancy/advisory role with Annexon Biosciences.

For additional information please reach out to Dr. Henk-Andre Kroon - hakroon@annexonbio.com

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