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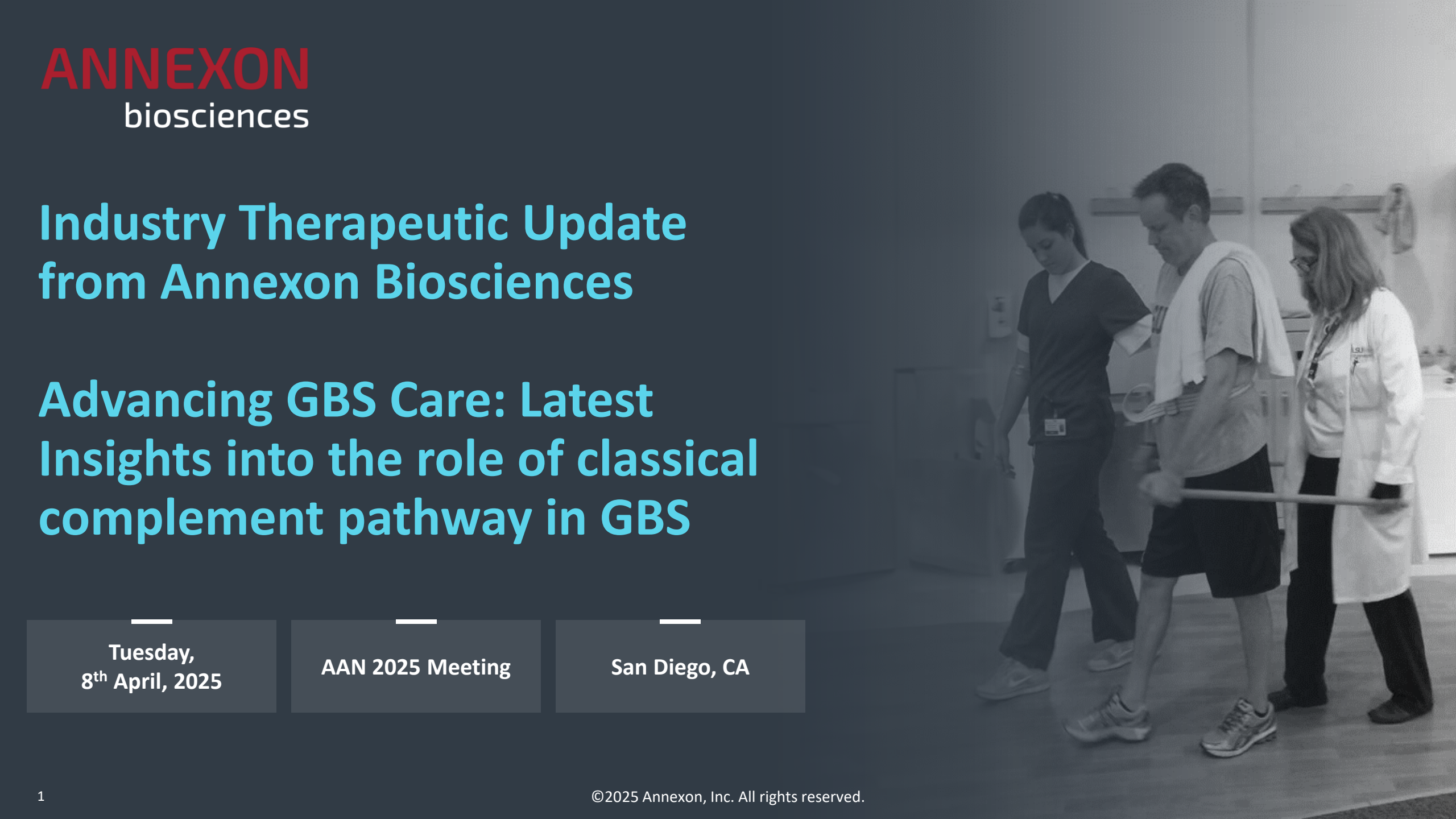
# Industry Therapeutic Update from Annexon Biosciences

# Advancing GBS Care: Latest Insights into the role of classical complement pathway in GBS



**Tuesday, 8th April, 2025**

**AAN 2025 Meeting**

**San Diego, CA**

# Symposium Goals and Objectives

- Address the risk of GBS as a neuromuscular emergency that requires early diagnosis and targeted treatment
- Discuss the role of C1q and neuroinflammation in the pathogenesis of GBS independent of GBS subtype
- Review the unmet needs in the current GBS treatment landscape
- Present results from the clinical trial program of tanruprubart (ANX005), a C1q inhibitor, in patients with GBS



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# Symposium Faculty

**Jeff A. Allen, MD**

**Professor of Neurology**

University of Minnesota

**Avni Kapadia, MD**

**Assistant Professor of Neurology**

Baylor College of Medicine

**Nick Silvestri, MD, FAAN**

**Professor of Neurology, Associate Dean**

University at Buffalo



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# Symposium Agenda

| Breaking New Ground In The Treatment Of Guillain-Barré Syndrome | | |
|---|---|---|
| **Time** | **Topic** | **Speaker** |
| 06:00 PM | Welcome & Introduction | Jeff Allen, MD |
| 06:15 PM | GBS Revisited | Avni Kapadia, MD |
| 06:30 PM | Role of Complement & Biomarkers in GBS Pathogenesis | Nick Silvestri, MD |
| 06:45 PM | The Treatment of Guillain-Barré Syndrome: New Insights into the role of C1q Inhibition | Jeff Allen, MD |
| 06:50 PM | Panel Discussion/Q&A | All |
| 07:00 PM | Closing | Jeff Allen, MD |



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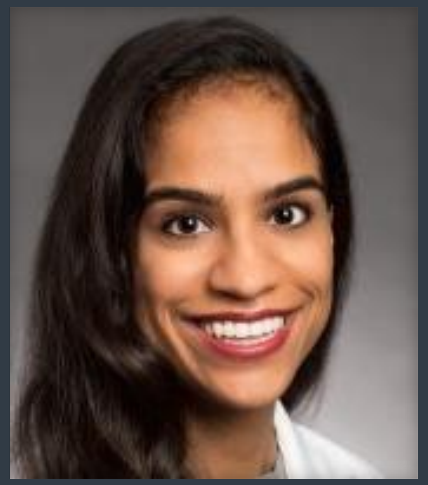
# Guillain-Barré Syndrome Revisited



**Avni Kapadia, MD**

**Assistant Professor of Neurology**

**Baylor College of Medicine**

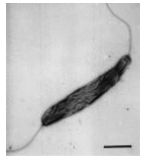
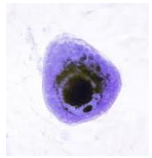
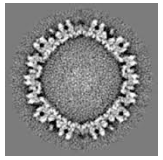
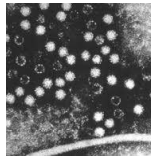
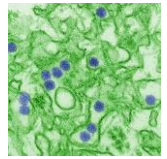
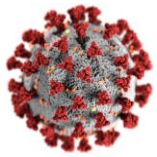
# Disclosures

Avni Kapadia is a consultant for Annexon.

# GBS is a Neuromuscular Emergency with Long-Term Disability

**Post-infectious Complement-mediated disease**

GBS is a post-infectious immune-mediated polyradiculoneuropathy[1,2]

| *Campylobacter jejuni* | *Cytomegalo virus* | *Epstein-Barr virus* | *Hepatitis E virus* | *Mycoplasma pneumoniae* | *Zika virus* | *SARS-CoV-2 virus* |
|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  |
| **30%** | **4%** | **1%** | **3%** | **10%** | **variable** | **rare** |

Complement-activating antibodies generated in response to the antecedent infection cross react to nerves leading to nerve damage[1,2]

GBS is the most common cause of acute paralytic inflammatory disease of the peripheral nervous system[1]

Nerve damage can lead to a range of symptoms including muscle weakness, numbness, pain, fatigue, and in severe cases acute paralysis[1]

**GBS develops rapidly, with patients typically presenting within a few days to weeks of symptom onset.**

[1]Willison HJ, et al. *Lancet*. 2016 Aug 13;388(10045):717-27. [2]Leonhard SE, et al. *Neurology*. 2022 Sep 20;99(12):e1299-e1313.



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# GBS Can Affect Anyone Of Any Age, Race, Or Sex At Any Time

**High unmet medical need**

- GBS is the most common cause of acute paralysis in the US[2]
- No FDA-approved therapies

**WORLDWIDE**
**≈150,000**
**cases per year[1]**
0.1% lifetime risk

**INCIDENCE IN US**
**≈6,000**
**cases per year[3]**

**Weaned from mechanical ventilation**

**Significant morbidity**

- Despite IVIg, GBS results in:
  - Severe weakness and paralysis[4]
  - Ventilation in 25% of patients[5,6]
  - 20% unable to walk unaided at one year[7]

GBS, Guillain-Barré syndrome; IVIg, intravenous immunoglobulin; MOA, mechanism of action. 1. van Doorn PA. *Presse Med*. 2013;42(6 Pt 2):e193-201; 2.. Willison HJ, et al. *Lancet*. 2016;388(10045):717-27; 3, Guillain-Barré Syndrome. US Centers for Disease Control and Prevention. Updated May 10, 2024. Accessed February 2, 2025. https://www.cdc.gov/campylobacter/signs-symptoms/guillain-barre-syndrome.html; 4. Bragazzi NL, et al. *J Neuroinflammation*. 2021;18(1):264; 5. Hughes RA, et al. *Cochrane Database Syst Rev*. 2014;2014(9):Cd002063; 6. van den Berg B, et al. *Nat Rev Neurol*. 2014;10(8):469-82; 7. Doets AY, et al. Regional variation of Guillain-Barré syndrome. *Brain*. 2018;141(10):2866-77.



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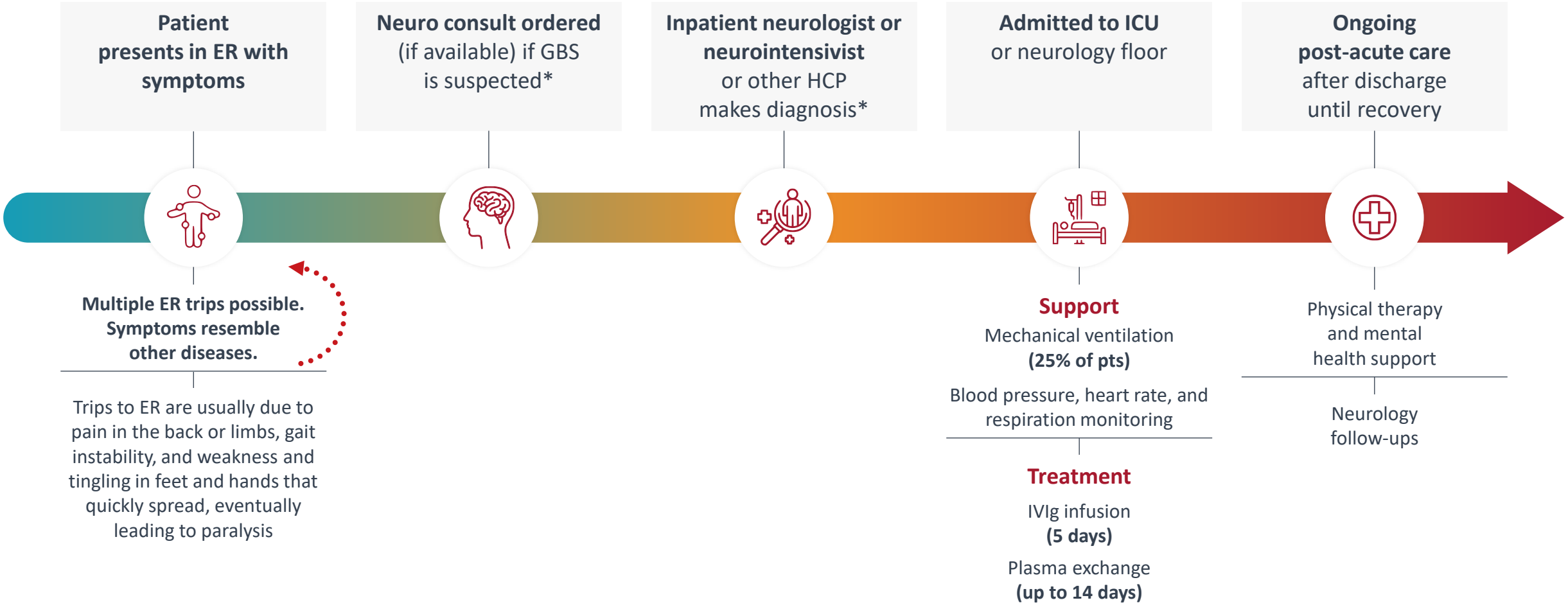
# The Prolonged Journey of Patients With GBS[1-3]




IVIg, intravenous immunoglobulin.

*Depending on institutional resources, the patient may not have access to a specialist. 1. van den Berg B et al. Nat Rev Neurol. 2014;10(8):469-482. 2. Dubey D et al. Muscle Nerve. 2016;53(3):384-387. 3. Shang P et al. Front Pharmacol. 2021;12:608130.





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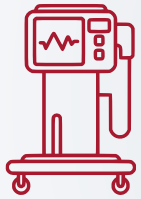
# GBS is Associated with Significant Acute Morbidity and Mortality

## 1 to 2 Months

Average hospitalization time for moderate or severe GBS[1]



## ≈1 in 4 Patients

Requires mechanical ventilation[2]

## In one study on ICU admission in patients with GBS[3]

- Median ICU time, overall: 21 days
- On ventilation, median ICU time: 28 days

## 1-Year Mortality Rates Range Geographically[4]

The Americas and Europe **5%**

Worldwide **2% to 17%**

**Up to 20%** **mortality rate for patients on ventilation**[5,6]

ICU, intensive care unit.

1. Harms M. *Neurohospitalist*. 2011;1(2):78–84. 2. van den Berg B et al. *Nat Rev Neurol*. 2014;10: 469–482. 3. Dhar R et al. *J Neurol* Sci. 2008;264(1-2):121-128. 4. Doets AY et al. *Brain*. 2018;141(10):2866-2877.
5. Fletcher DD et al. *Neurology*. 2000;54:2311-2315. 6. Netto AB et al. *Ann Indian Acad Neurol*. 2011;14(4):262-266.





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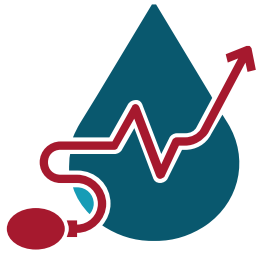
# GBS Is Associated With Significant Long-Term Morbidity

## AT 3 YEARS [1,2]

**71%**
experience neuropathic pain

**50%**
have autonomic dysfunction



**4%**
are unable to walk unassisted

**2%**
are bedridden

## AT 10 YEARS[3]

**Up to 52%**
Have disability (eg, residual weakness, numbness)

## AT 20 YEARS[4]

**42%**
Experience severe fatigue

**IRREVERSIBLE DISABILITY CAN HAVE AN IMPACT ON SOCIAL LIFE AND ABILITY TO PERFORM ACTIVITIES OF DAILY LIFE[3]**

1. Uz FB et al. *Malawi Med J*. 2023;35(3):156-162. 2. Martic V et al. *Can J Neurol Sci*. 2018;45(3):269-274. 3. Forsberg A et al. *J Neurol Sci*. 2012;317(1-2):74-79. 4. Drory VE et al. *J Neurol Sci*. 2012;316(1-2):72-75.





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# GBS Case Report- Part I

**JT, a 51-year-old female, arrived at the emergency department complaining of weakness and discomfort in her extremities.**

JT explained she had been feeling numbness and tingling in her toes for the past two weeks, with symptoms progressively worsening. About one week prior, JT returned from an overseas trip and attributed her current symptoms as residual effects of an illness she experienced towards the end of her travels.

Over the past 3 days, JT had experienced increased weakness and impaired motor skills. She noted a specific difficulty holding her toothbrush and brushing her teeth, influencing her to seek medical attention.

Due to her rapidly progressing signs and symptoms, JT was admitted to the hospital. JT had stable vital signs, breathing independently on room air, and due to suspicion for GBS, CSF studies were obtained and demonstrated elevated protein.

JT was diagnosed with GBS and was started immediately on IVIg 0.4g/kg for a 5-day course.

# GBS Case Report- Part II

JT's status worsened the next 24-48 hours while on the inpatient neurology ward, and had trouble breathing and swallowing.

JT was admitted to the ICU on day 2 of her 5-day course of IVIg where she was provided with respiratory support to assist with breathing, and a nasogastric (NG) tube to provide nutrition.

On day 9 since the start of IVIg, JT began to show significant signs of improvement in her respiratory status

JT was transferred from the ICU to the hospital's step-down unit where her condition stabilized.

After one week in the ICU and another week on the inpatient service for therapy and respiratory monitoring, she was discharged to inpatient rehabilitation for ongoing post-acute care.

She continued comprehensive PT/OT during her rehab stay, and she was referred to neurology & PMR for outpatient follow up.



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# Current Treatments' Effects on Immune Activity in patients with GBS

## IVIg[1,2]

- **Treatment time:** 5 days
- Nontargeted immunomodulation
- A second dose has not been shown to be effective, but may be given in patients experiencing treatment fluctuations
- Contraindications: renal deficiency or CHF

## PLASMA EXCHANGE[1,2]

- **Treatment time**: 5 to 14 days
- Central line may be required
- Experienced team required
- Contraindications: septic shock or MI within 6 months

- Use of IVIg and PE is largely based on GBS clinical guidelines established through observational studies which have shown IVIg and PE may hasten recovery.[2]
- A Cochran analysis found no adequate comparisons of IVIg with placebo in adults, but did find moderate quality evidence that, in severe disease, IVIg started within two weeks from onset hastens recovery as much as PE.[2]

CHF, congestive heart failure; DVT, deep vein thrombosis; HFGS, Hughes functional grading scale; MI, myocardial infarction; PRES, posterior reversible encephalopathy syndrome; TRALI, transfusion-related acute lung injury;
*Treatment-related fluctuations refers to improvement in the HFGS score of ≥1 grade after completion of immunotherapy followed by worsening of the HFGS score of at least 1 grade within the first 2 months after disease onset. †TRALI is a rare and devastating complication of transfusion, defined as acute-onset respiratory distress after administration of blood products. IVIg-associated TRALI may contribute to accelerated deterioration or worse outcomes in some patients with GBS. *Not enough data to support second/prolonged dosing with IVIg

1. Shang P et al. *Front Pharmacol*. 2021;12:608130. 2. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. Cochrane Database Syst Rev. 2014 Sep 19;2014(9):CD002063.





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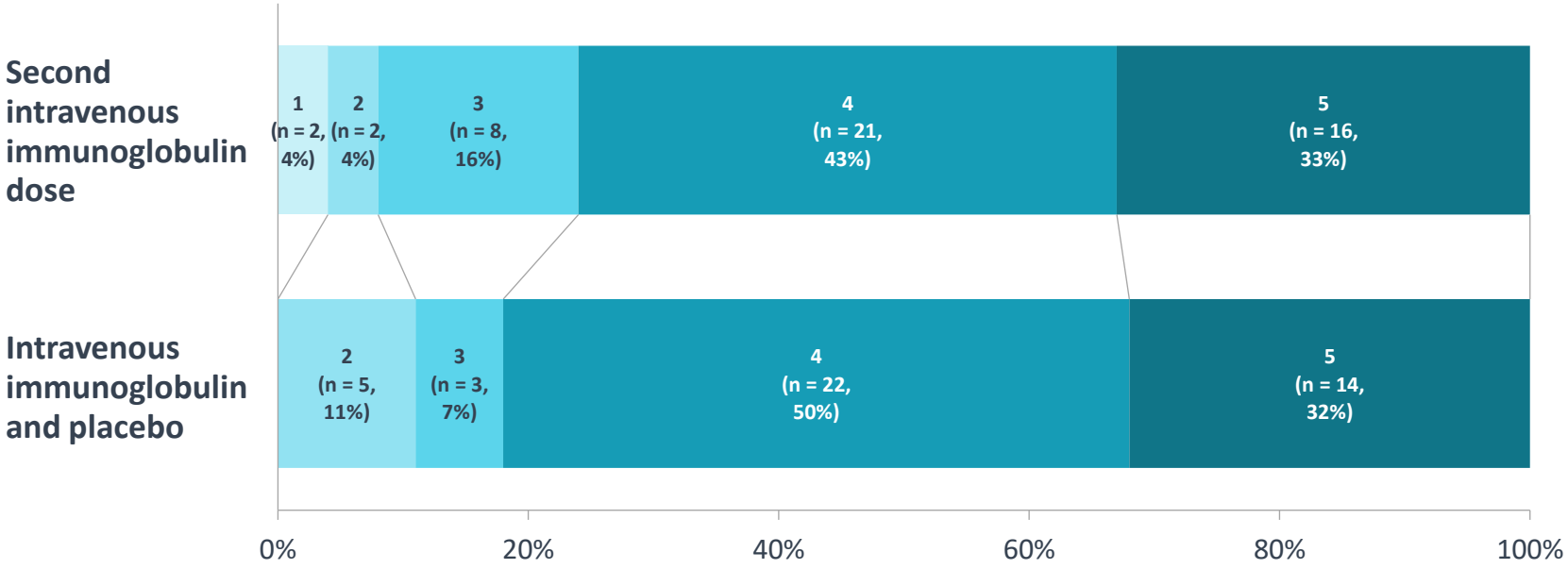
# SID-GBS Trial Evaluated 2nd course of IVIg in Patients with GBS with Poor Diagnosis

## Key Study Outcomes

- **No improvement in disability** at week 4 in re-treated group
- **More SAEs** (35% vs 16%) in re-treated group
  - Including thromboembolic events
  - N=4 died in the intervention group

## Guillain-Barré Syndrome Disability Score




**Guillain-Barré syndrome disability score at 4 weeks in the modified intention-to-treat population**

Adapted from: Walgaard C et al. Lancet Neurology 2021


[1]Walgaard C et al. Lancet Neurology 2021. [2]Tilburg SJ, et al. *Ann Clin Transl Neurol* 2025.

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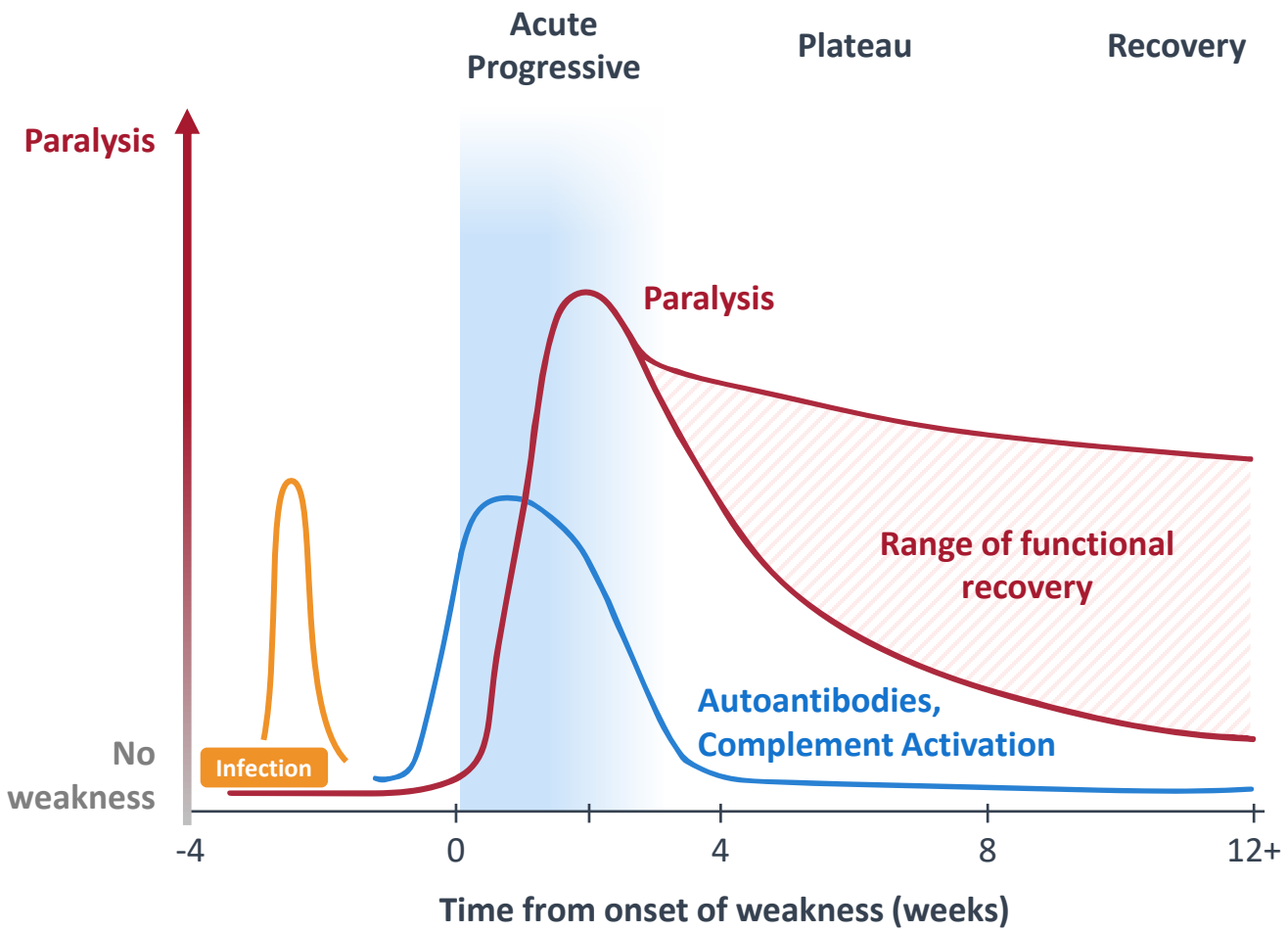
# The Active Disease Phase Defines The Key Treatment Window

## Acute disease phase of GBS is generally short and varies by patient




**Acute Progressive Phase:**

- Rapidly progressive bilateral muscle weakness peaking by 1 week in most cases and lasting up to 4 weeks

**Plateau Phase:**

- May include extended period of ventilation in ICU and intensive support care lasting weeks to months

**Recovery Phase:**

- Gradual muscle strength and functional improvement occurring over weeks to years as nerves repair

Adapted from van den Berg B et al. *Nat Rev Neurol*. 2014;10(8):469-482. and Leonhard SE et al. *Nat Rev Neurol*. 2019;15(11):671-683.



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# Role of Complement & Biomarkers in GBS Pathogenesis

**Nick Silvestri, MD, FAAN**

**Professor of Neurology, Associate Dean**

**University at Buffalo**

# Disclosures

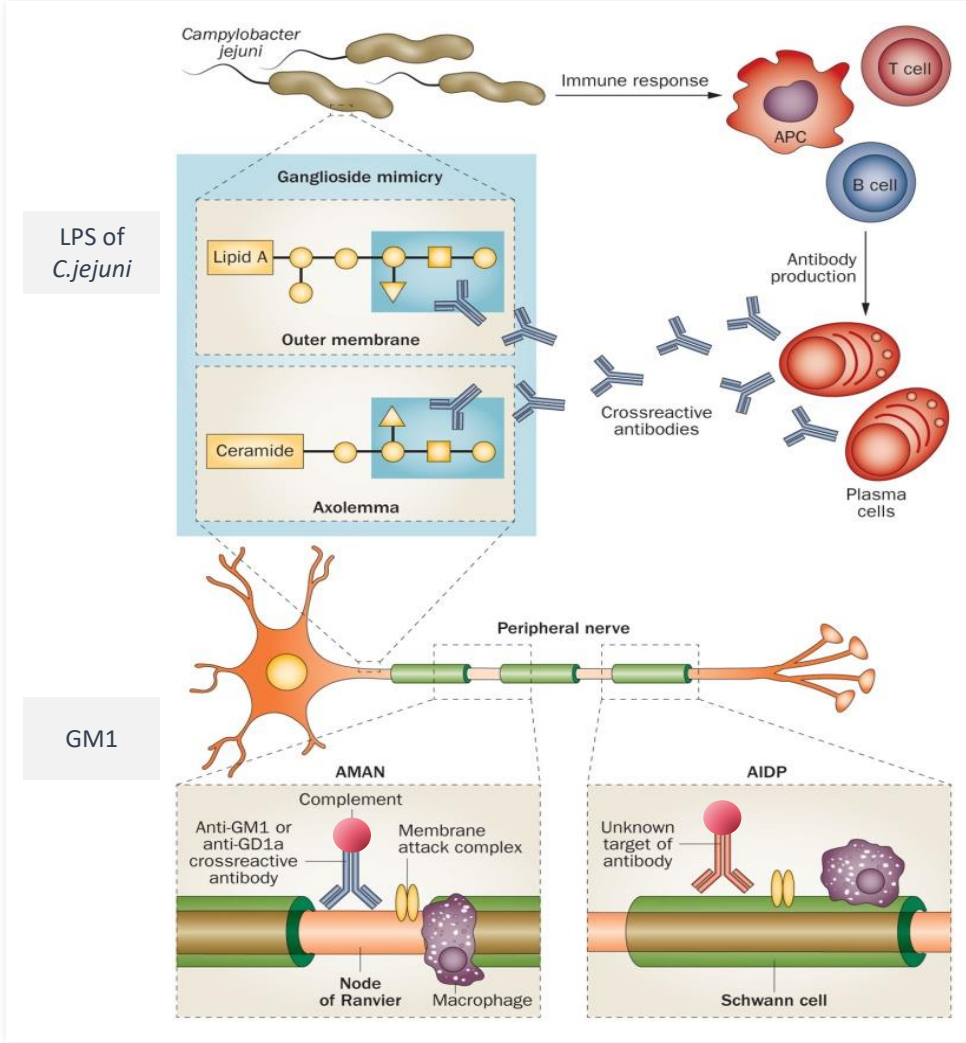
Nick Silvestri is a consultant for Alexion, Amgen, Annexon, argenx, Immunovant, Johnson & Johnson, UCB and a speaker for Alexion, argenx, UCB, and Takeda.

# Autoantibodies Link the Trigger to Complement Mediated Nerve Damage in GBS

Antibodies generated against the antecedent infection **cross-react** with a range of glycolipids in myelin and axonal membrane

Antibodies bound to nerve cells **activate complement**

Complement activation causes neuroinflammation, nerve damage and destruction leading to common manifestations of GBS – **functioning as a common pathway across all GBS types**




[1]Van den Berg et al., 2014; [2]Halstead et al., 2016



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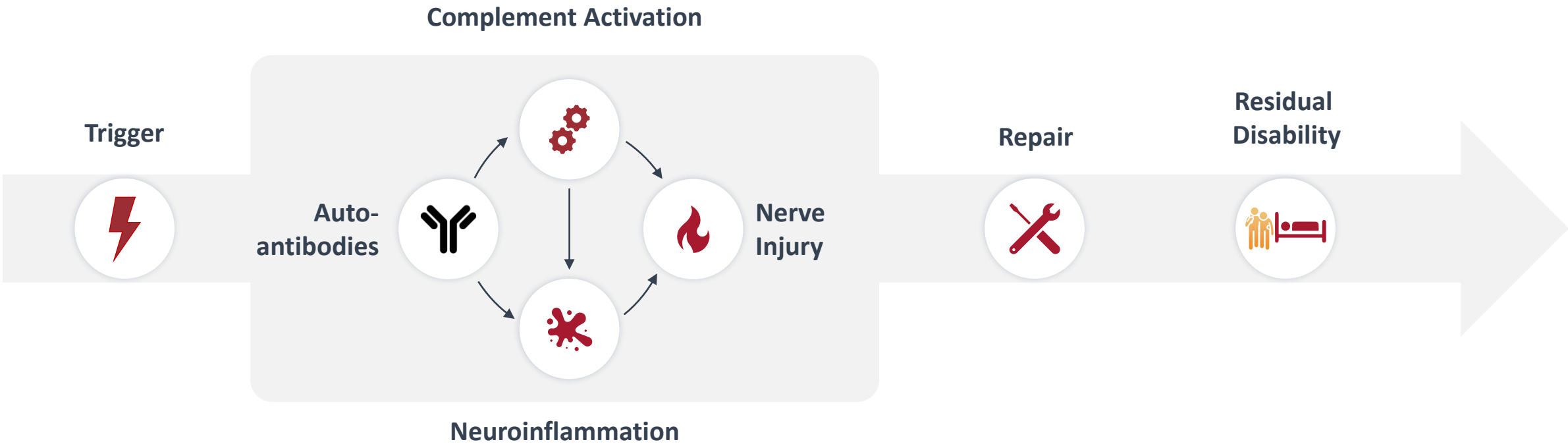
# Characterizing the Time Course of GBS

## Degree of Nerve Damage During Acute Phase Determines Functional Outcome




Min YG, et al., Timing of intravenous immunoglobulin treatment and outcome in Guillain–Barré syndrome: Is time nerve? Muscle & Nerve. 2024;70(6):1215-1222



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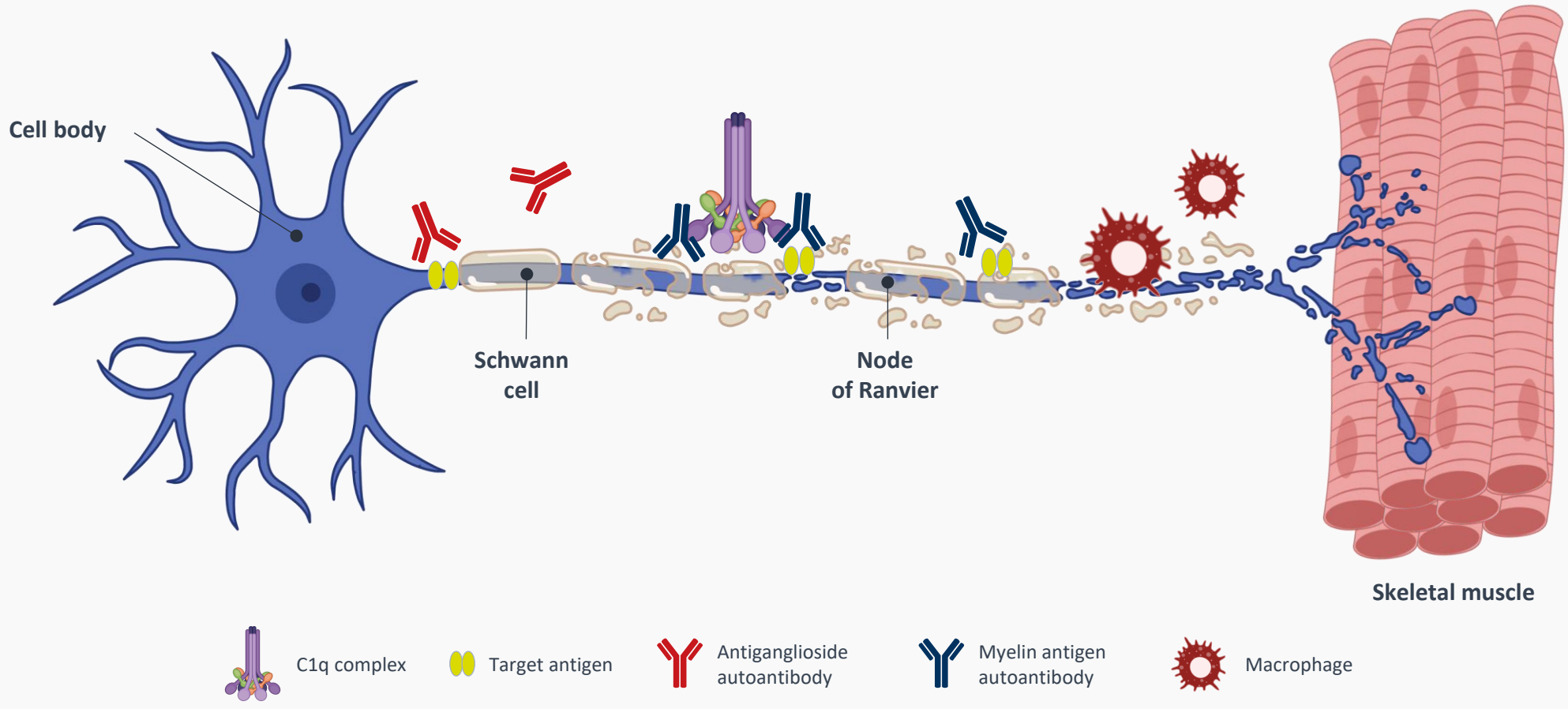
# Complement Is a Key Mediator of Neuroinflammation and Nerve Destruction in GBS [1,2]

## C1q binds to IgG & IgM antibodies on nerve, activates classical complement pathway




IgG, immunoglobulin G; IgM, immunoglobulin M. 1 Misawa S, Suichi T. *Clin Exp Neuroimmunol.* 2020;11(2):90-93. 2 Dalakas MC et al. *Nat Rev Neurol.* 2020;16(11):601-617.



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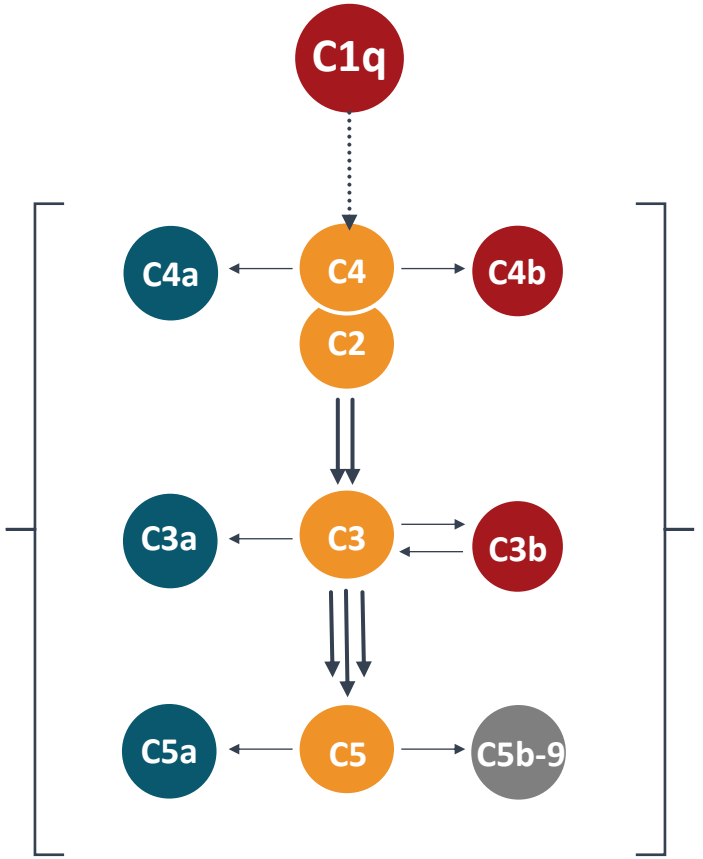
# C1q Drives Harmful Neuroinflammation and Nerve Damage

**C1q Is the Initiating Molecule of the Classical Complement Pathway**

C1q anchors to auto-antibodies on nerve surface and activates pathway

## INFLAMMATION AND EDEMA

Local, immediate, complement and '1st responder' driven




## NERVE DAMAGE & DESTRUCTION

Recruitment of destructive cells including macrophages

**1.** Lansita, et al., 2017; DOI: 10.1177/1091581817740873





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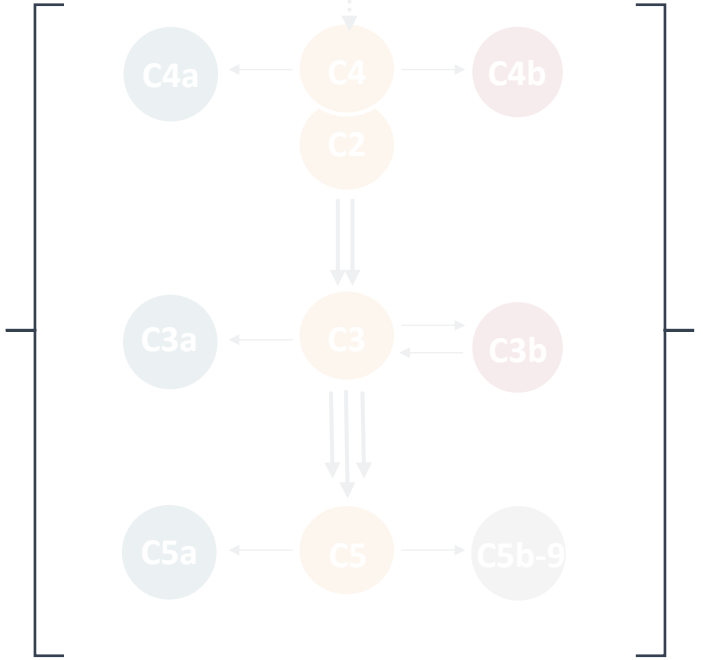
# C1q Drives Harmful Neuroinflammation and Nerve Damage

**Tanruprubart Rapidly Shuts Down Activation of the *ENTIRE* Classical Complement Pathway on the Nerve**

**Tanruprubart**




## IMMEDIATE CESSATION OF INFLAMMATION AND EDEMA

## HALT NERVE DAMAGE & DESTRUCTION

Allow for recovery phase and repair of damaged nerves

**1.** Lansita, et al., 2017; DOI: 10.1177/1091581817740873





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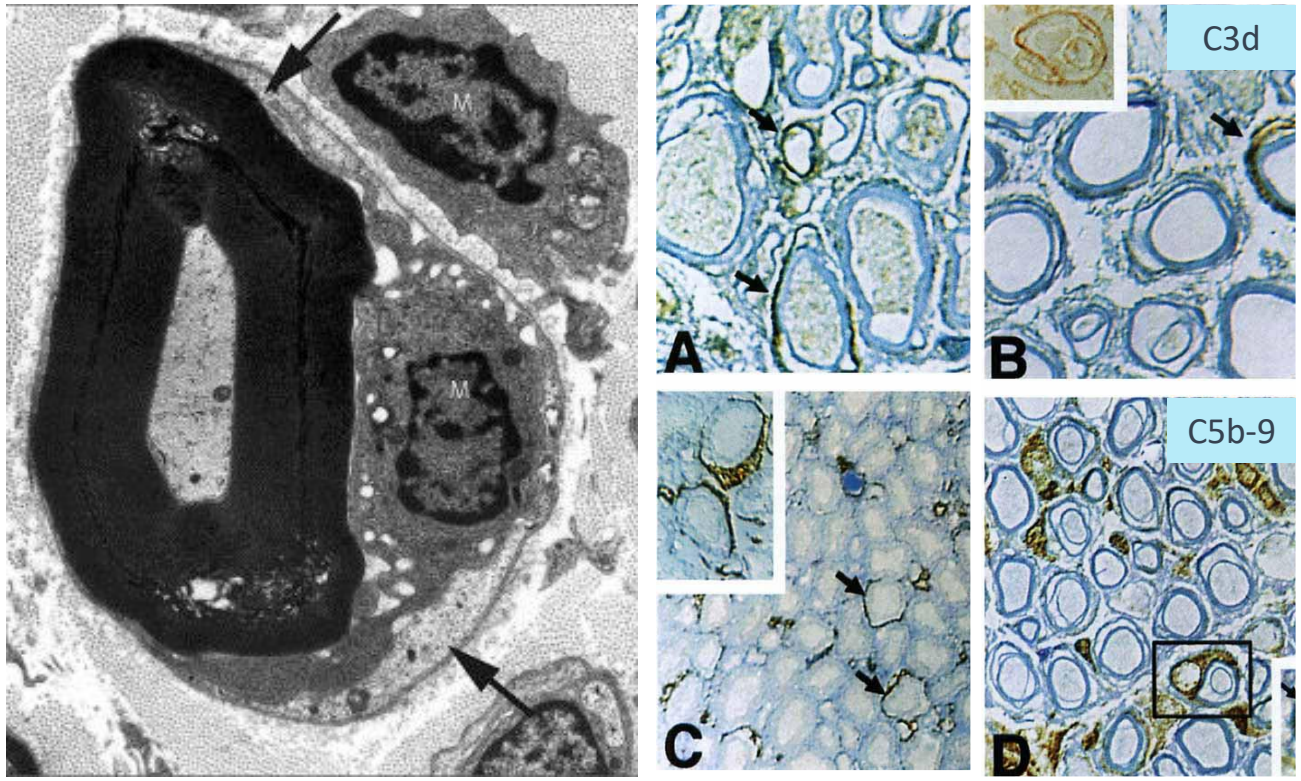
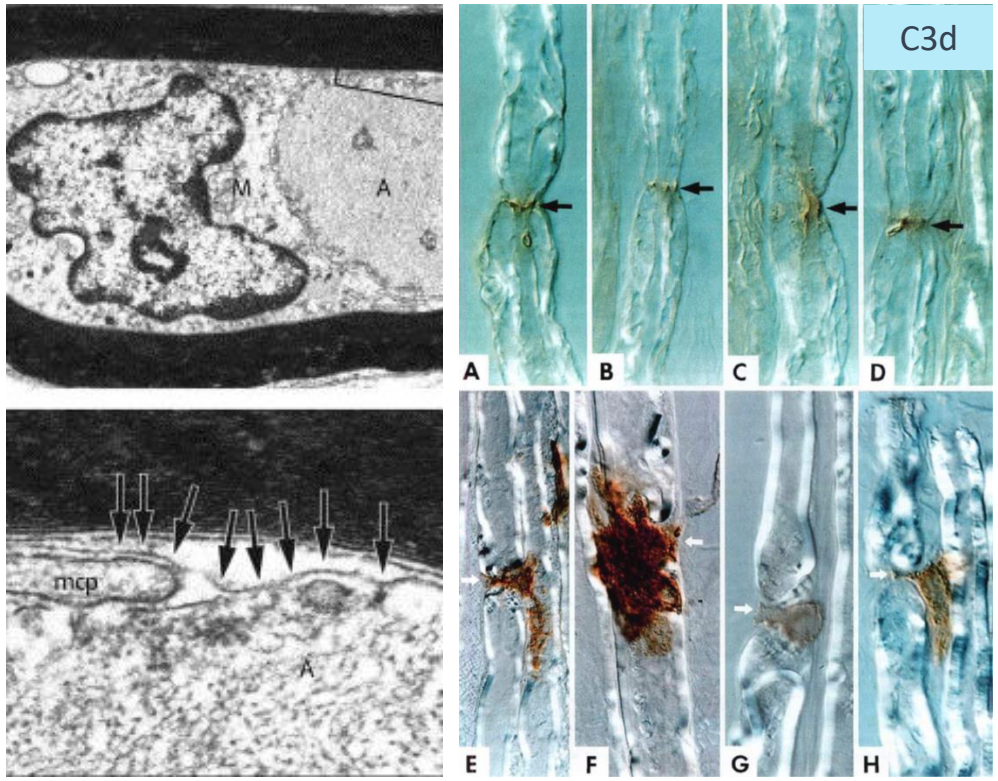
# The Role of Complement in GBS Subtypes

## C1q is activated by autoantibodies on axon and myelin

### Acute Inflammatory Demyelinating Polyneuropathy (AIDP)




### Acute Motor Axonal Neuropathy (AMAN)




[1]Griffin et al. Ann Neurol 1994, 2Hafer-Macko et al. Ann Neurol 1997



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# What is the Relevance of GBS Subtypes for Treatment?

Histopathology rarely available

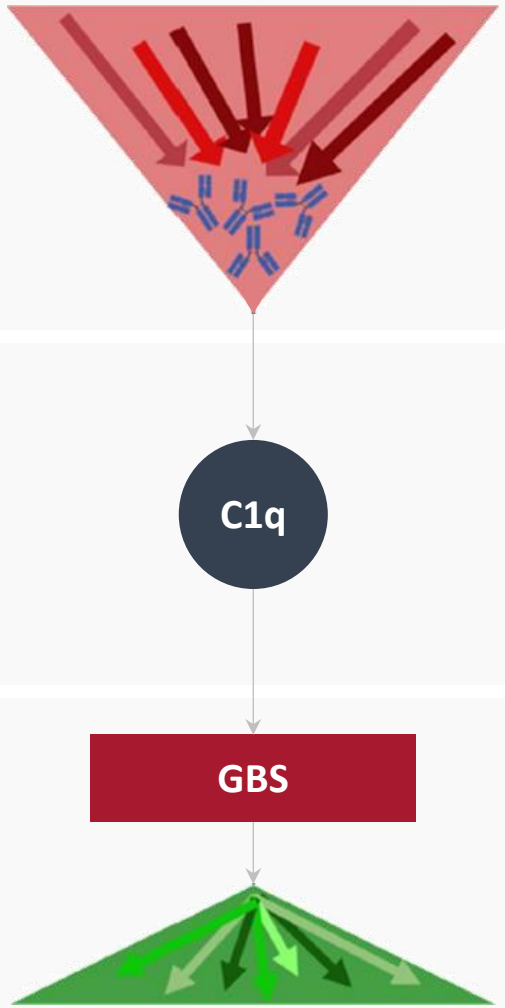
Nerve conduction studies

- Various sets of criteria in use
- Frequently equivocal subtype
- Subtype classification may change over time

Complement activated by C1q is involved in all subtypes (AMAN & AIDP)

Treatment is the same

Limited independent prognostic value




Variability in antecedent infection and regional environment factors

Complement-fixing autoantibodies against different nerve complements

C1q is a key, innate amplifier of antibody function, driving inflammation and nerve damage

Defined spectrum of clinical manifestations and outcomes



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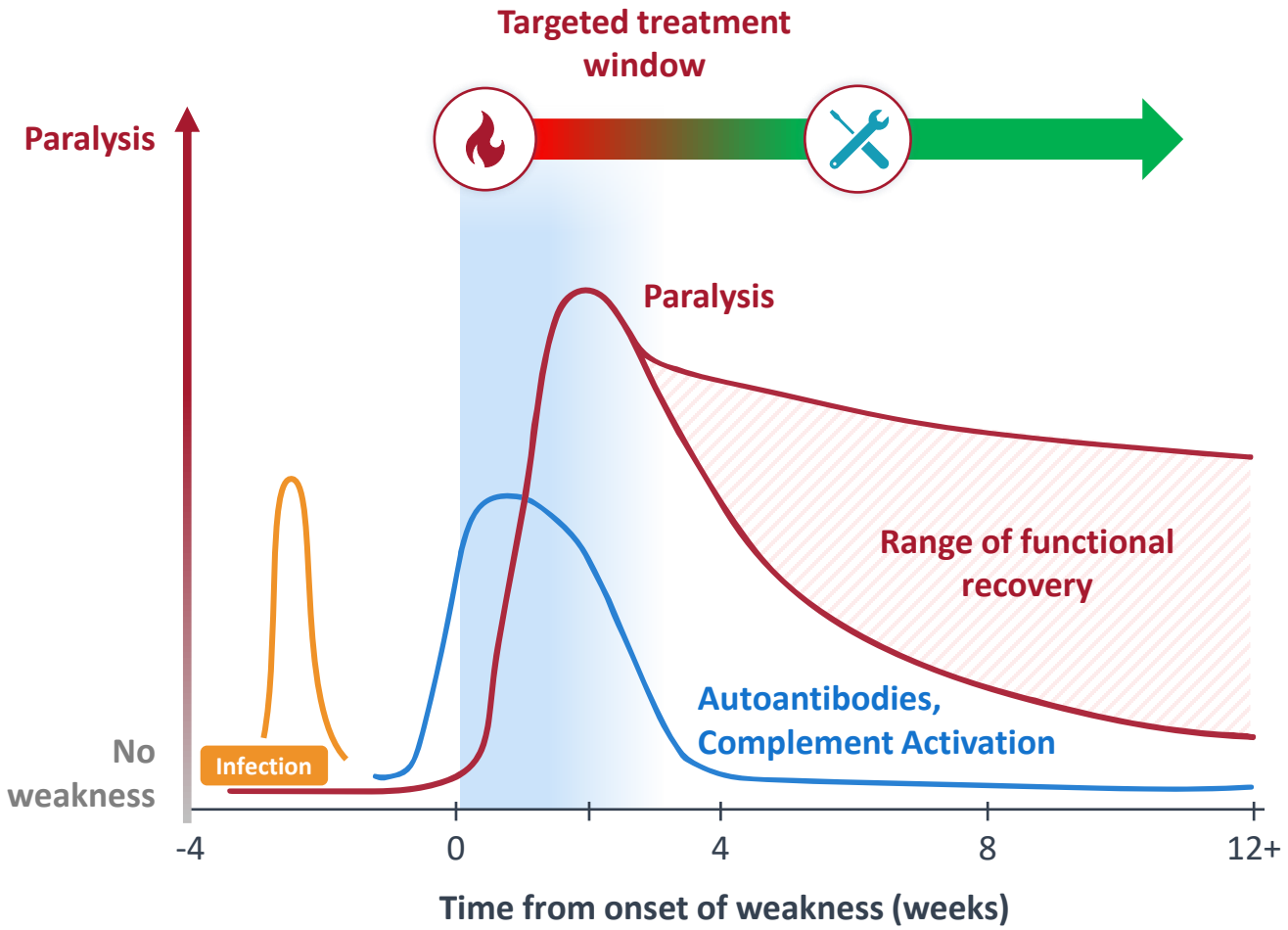
# Finding the Balance in GBS – Anti-inflammatory and Pro-Healing

## Acute disease phase varies by patient but is generally short




### Objectives of anti-C1q treatment in GBS

- **Block** complement-mediated nerve neuroinflammation, nerve damage and destruction during the acute disease
- **Do not block** complement during the healing phase when normal immune function is required

### Target treatment window is likely short

[1]van den Berg et al Nat Rev Neurol. 2014;. [2]Leonhard SE et al Nat Rev Neurol. 2019



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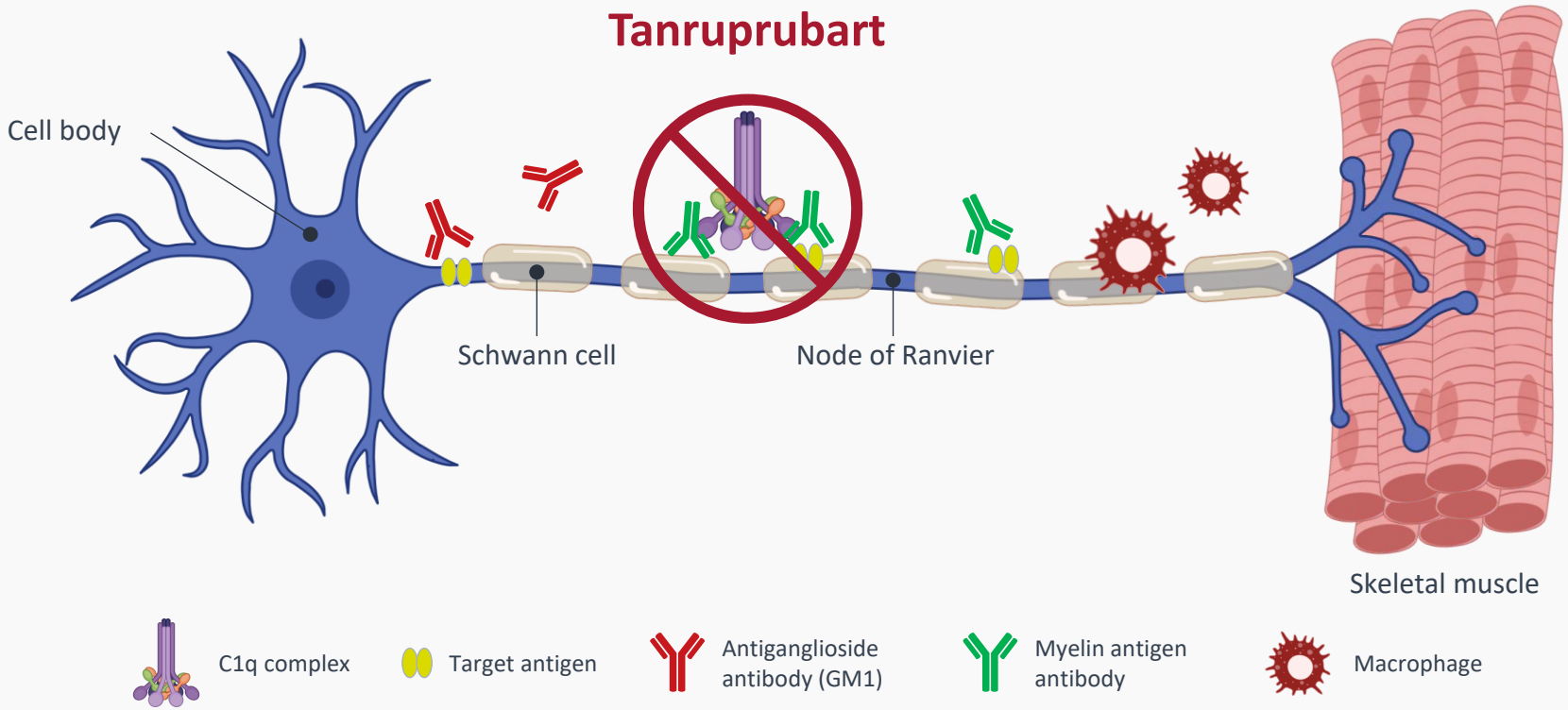
# The Treatment of Guillain-Barré Syndrome: New Insights into the role of C1q Inhibition

**Jeff A. Allen, MD**
**Professor of Neurology**
**University of Minnesota**
**Minneapolis, Minnesota, USA**

# Disclosures

Jeff Allen is a consultant for Alexion, Annexon, Alnylym, AstraZeneca, Argenx, Octaphama, CSL Behring, Takeda, Pfizer, Immunopharma, Immunovant, Grifols, Sanofi, and Johnson & Johnson.

# A Single Dose of Tanruprubart (ANX005) Is Designed to Target C1q, Stopping the Classical Complement Pathway Where It Starts




**Tanruprubart and its uses are investigational and have not been approved by the U.S. Food and Drug Administration. This information is presented only for purposes of providing a general overview of clinical trials and should not be construed as a recommendation for use of any product for unapproved uses.**

1. Lansita JA et al. *Int J Toxicol*. 2017;36(6):449-462. 2. Misawa S, Suichi T. *Clin Exp Neuroimmunol*. 2020;11(2):90-93. 3. Dalakas MC et al. Nat Rev Neurol. 2020;16(11):601-617.





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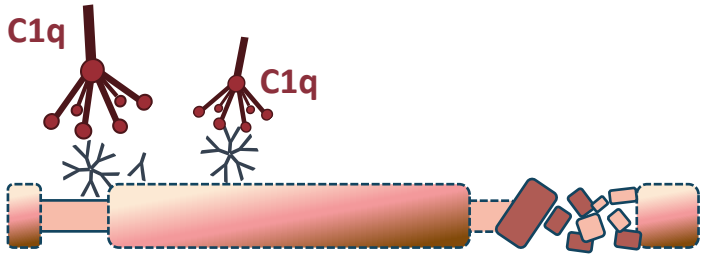
# Early and Rapid C1q Inhibition has the Potential to Slow Nerve Damage

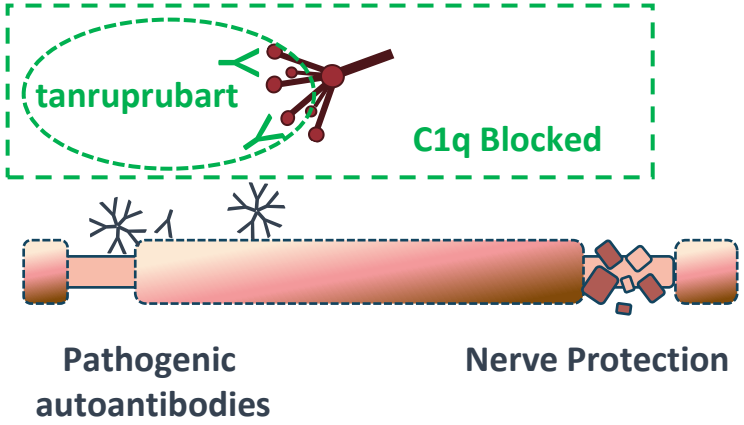
## GBS Active Disease Phase
*Complement mediates nerve damage*

**C1q** ➡
- Classical complement activation
- Nerve fiber damage
- Tissue debris



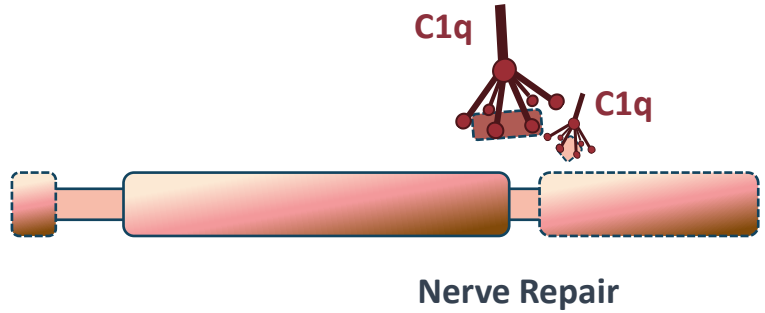

## Tanruprubart During Effective Treatment Window

**C1q** ➡
- Full cascade blocked by tanruprubart
- 30mg/kg leads to 1 week of C1q suppression during active disease




## GBS Recovery Phase
*Complement facilitates nerve repair*

**C1q** ➡
- Clears debris
- Allows nerve regeneration
- Facilitates remyelination & repair

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Hafer-Macko C et al., (1996) Ann Neurol 39 & 40

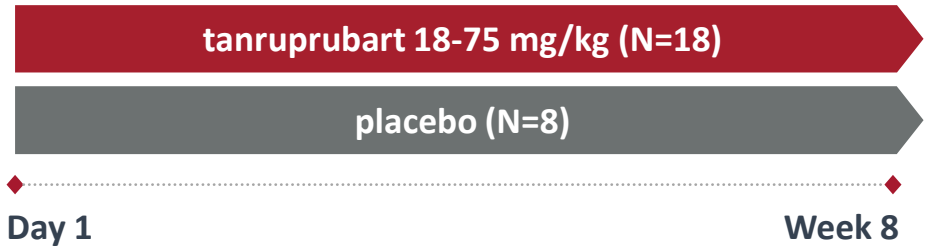


ANNEXON biosciences

# The Dose-Ranging Ph1b Study Laid Foundation for Phase 3 Trial

## Phase 1b Study Design

**Study Schematic**




- Randomized, double-blind, placebo-controlled study
- N=26[1] Adults with GBS in Bangladesh
- Mean time from onset of weakness: 8.1 days
- Mean GBS-DS at baseline: 4[1]

## Key Learnings Applied to Phase 3

- Test 2 doses to evaluate efficacy with the lower dose
- Stratify by key prognostic factors
  - MRC sumscore
  - Time from onset of weakness
- Treat as early as possible (day of randomization)

**Phase 3 Designed to Define the Appropriate Duration of Complement Inhibition in GBS**

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[1]18-75mg/kg double-blinded dose cohorts



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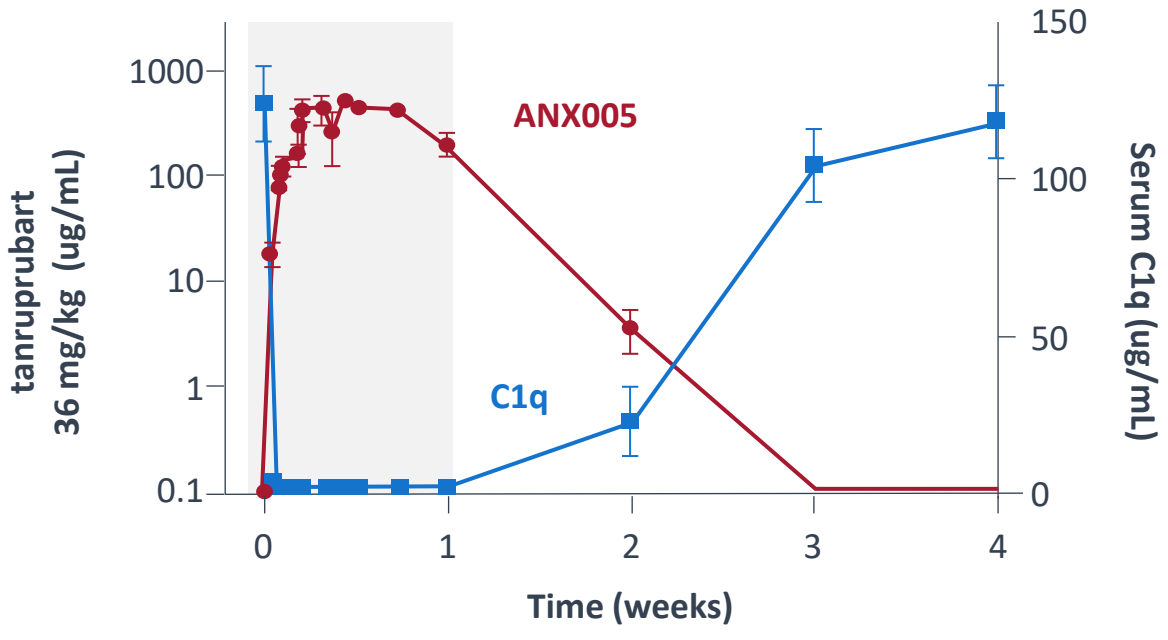
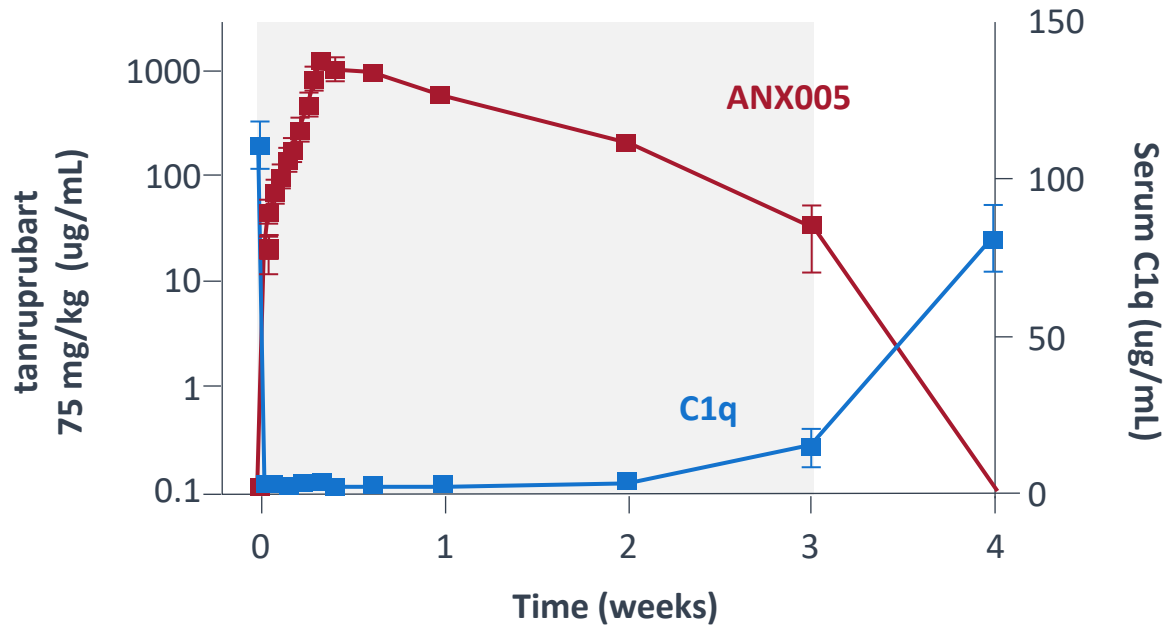
# Single Dose of Tanruprubart Blocks Complement on Day 1 Independent of Dose

## Shorter C1q Inhibition (36 mg/kg)




## Longer C1q Inhibition (75 mg/kg)

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# Pivotal Phase 3 Trial Design

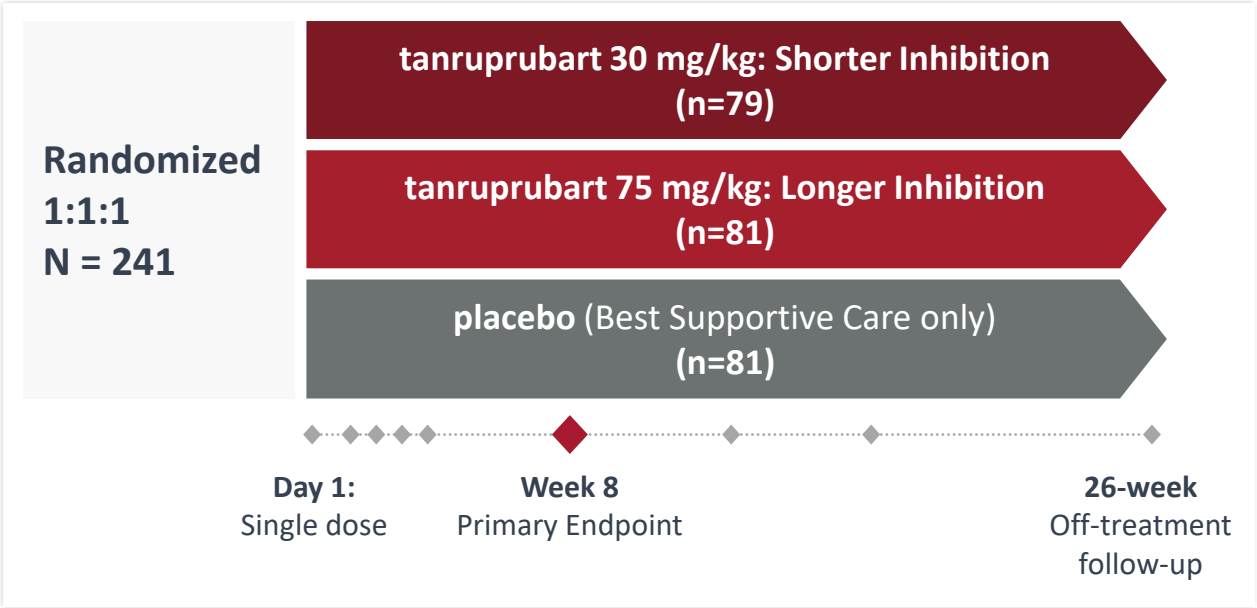
## Randomized, Double-Blind, Placebo-Controlled Study

### Patient Selection

- GBS Disability Score 3, 4 or 5
- <10 days from onset of weakness
- Not eligible to receive IVIg or PE
- Stratified by baseline prognostic factors: muscle strength and time from onset of weakness

### Key Endpoints

| | |
|---|---|
| **Primary Outcome Measure** | GBS-DS at Week 8 analyzed using a 3-level proportional odds model |
| **Secondary Endpoints** | Muscle strength (MRC sumscore), Motor Disability (ONLS), Duration of Ventilation |




**Conducted at sites in Bangladesh and the Philippines**

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# GBS Disability Scale (GBS-DS) is Used to Assess the Functional Status in Patients With GBS

## GBS-DS GRADES[1]


**Lower muscle strength, as evaluated by the MRC sum score, correlates with higher GBS-DS grade.[1,2]**

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GBS-DS, GBS disability score; MRC, Medical Research Council.. 1. van Koningsveld R et al. *Lancet Neurol.* 2007;6(7):589-594. 2. Kleyweg RP et al. *Muscle Nerve.* 1991;14(11):1103-1109.



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# GBS-DS 3-Point Scale (Trichotomy) Used in Assessing Treatment Benefit

## GBS-DS is a Well-Accepted Endpoint

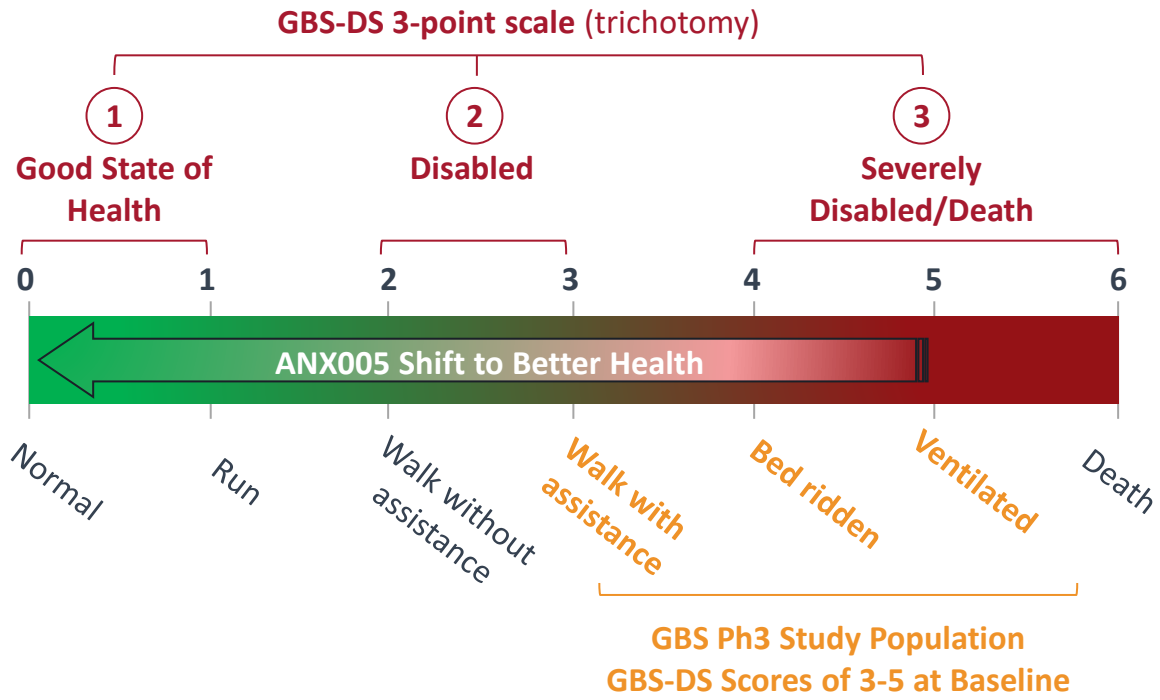
### GBS-DS Overview

- Validated endpoint that assesses functional status of patients with GBS
- Consists of 7 mutually exclusive grades: 0 (healthy) to 6 (death)
- FDA alignment to use GBS-DS as Ph3 Primary Endpoint at week 8

### GBS-DS Scale Collapsed into 3 Categories Enhances Clinical Interpretability

- **Approach:** Collapse 7-point scale to a 3-point scale (trichotomy)
  - 0-1: Good State of Health
  - 2-3: Disabled
  - 4-6: Severely Disabled/Death
- **Rationale:**
  - ✓ **Enhances clinical interpretability** by focusing on **a subject's actual health status at week 8** after receiving tanruprubart or placebo

### GBS-DS Scale for Pivotal Phase 3

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# Baseline Characteristics Similar and Well Balanced Across Treatment Groups

## Stratified by Key Prognostic Factors: MRC Sumscore and Time Since Onset of Weakness

| Baseline Characteristic | placebo (n=81) | tanruprubart 30mg/kg (n=79) | tanruprubart 75mg/kg (n=81) |
|---|---|---|---|
| **Age at screening, 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 score, n (%)** | | | |
| 3 Able to walk 10 meters across open space with help | 7 (8.6) | 12 (15.2) | 10 (12.3) |
| 4 Bedridden or chair bound | 64 (79.0) | 56 (70.9) | 60 (74.1) |
| 5 Requiring assisted ventilation for at least part of the day | 10 (12.3) | 11 (13.9) | 11 (13.6) |
| **Baseline MRC sumscore (range, 0-60), n (%)** | | | |
| 0-20 | 38 (46.9) | 38 (48.1) | 37 (45.7) |
| 21-60 | 42 (51.8) | 41 (51.9) | 44 (54.3) |
| **Time since of onset of weakness to treatment** | | | |
| Days, mean (SD) | 6.5 (1.7) | 6.3 (1.9) | 6.6 (2.0) |
| **Electrophysiology 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) |

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AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; GBS-DS, Guillain-Barré Syndrome Disability Score; MRC, Medical Research Council.



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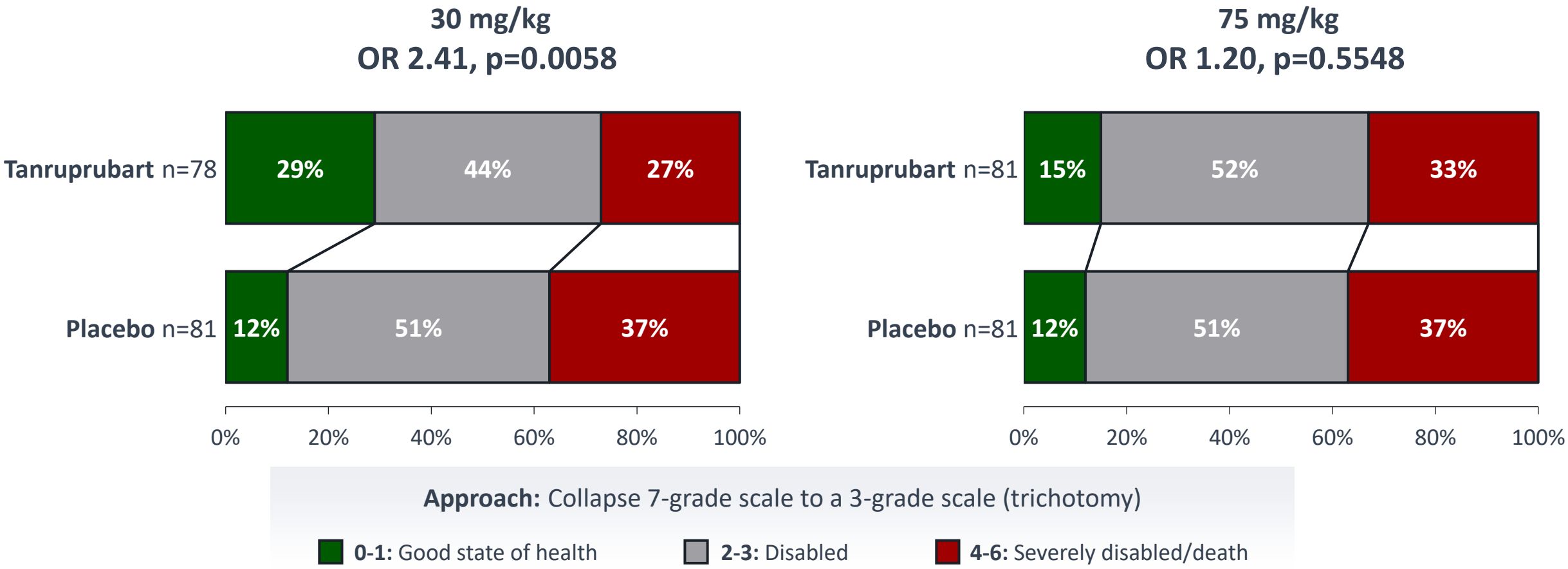
# Primary Endpoint: tanruprubart 30 mg/kg Showed Significant Improvement on GBS-DS at Week 8

## Primary Endpoint: 2.4-Fold Higher Likelihood of Being in a Better State of Health Relative to Placebo

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GBS-DS, Guillain-Barré Syndrome Disability Score; OR, odds ratio.





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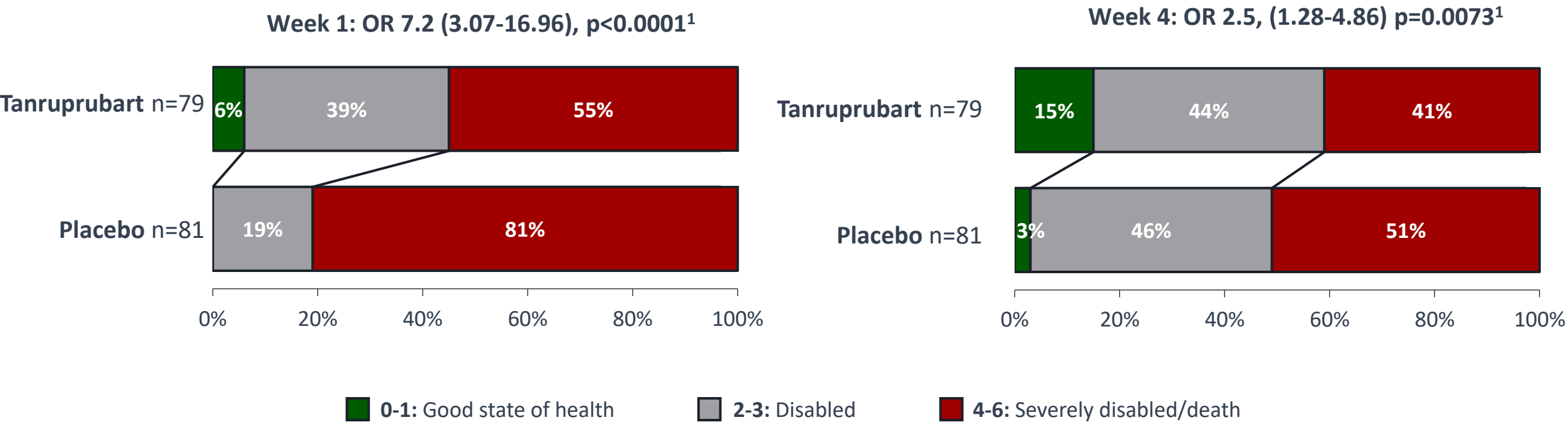
# Treatment Effect with Tanruprubart 30 mg/kg on GBS Disability Scale During the Early Phase of GBS

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[1]Nominal



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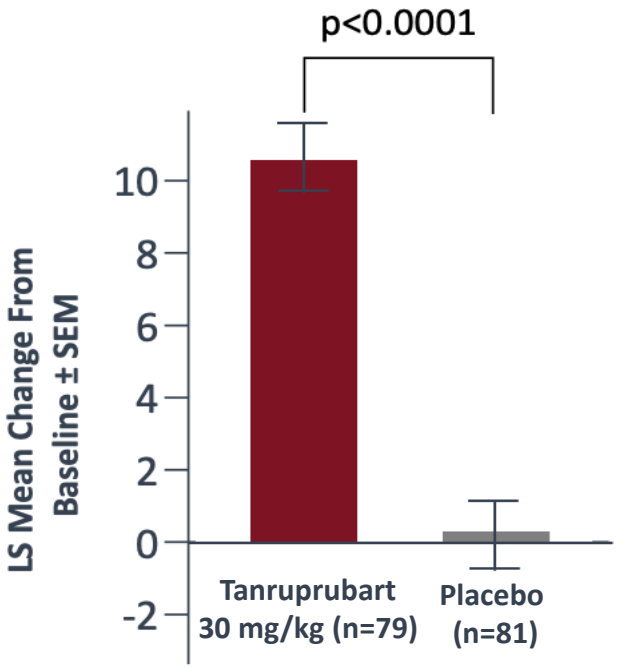
# Tanruprubart (ANX005) 30 mg/kg Provided Early Recovery of Muscle Strength and Motor Function

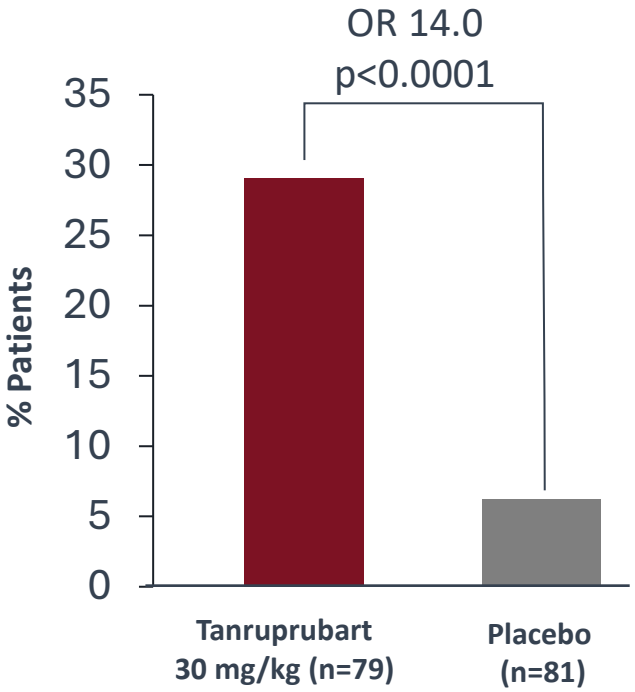
## MORE THAN A 10-POINT IMPROVEMENT IN MUSCLE STRENGTH (MRC SUMSCORE)[1] OVER PLACEBO AT WEEK 1

MUSCLE STRENGTH




## 14 TIMES MORE LIKELY TO PERFORM TIMED UP AND GO (TUG) AT WEEK 1

MOTOR FUNCTION

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[1]LS mean point improvement relative to placebo



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# Treatment Effects of Tanruprubart 30 mg/kg vs. Placebo

| Pre-specified Analyses | Unit | At Week 1 | | At Week 4 | | At Week 8 | | Through Week 26 (MMRM) | |
|---|---|---|---|---|---|---|---|---|---|
| **GBS-DS** | Odds Ratio | OR[1]: 7.22 | p<0.001[3] | OR[1]: 2.49 | p=0.0073[3] | **OR[1]: 2.41** | **p=0.0058** | OR[1]: 1.49 | p=0.0120[3] |
| **MRC** | Point Improvement | **10 points[2]** | **p<0.0001[3]** | 5.4 points[2] | p=0.0026[3] | **4 points[2]** | **p=0.0351[3]** | 5.4[2] | p=0.0010[3] |
| **ONLS** | Point Improvement | -2.1 points[2] | p<0.0001[3] | -1.1 points[2] | p=0.0154[3] | **-0.8 points[2]** | **p=0.0965[3]** | -1.1[2] | p=0.0063[3] |
| **Ventilation** | Median Days | N/A | | | | | | **28 days reduction[4]** | **p=0.0356[3]** |

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[1] Odds Ratio: Likelihood that a patient on ANX005 is in a better state of health relative to placebo
[2] LS mean difference relative to placebo
[3] P-values for nominal testing using 2-sided $\alpha$=0.05
[4] For those requiring ventilation
[5] LS Mean percent reduction
GBS-DS, Guillain-Barré Syndrome Disability Score; MRC, Medical Research Council; ONLS, overall neuropathy limitations scale.



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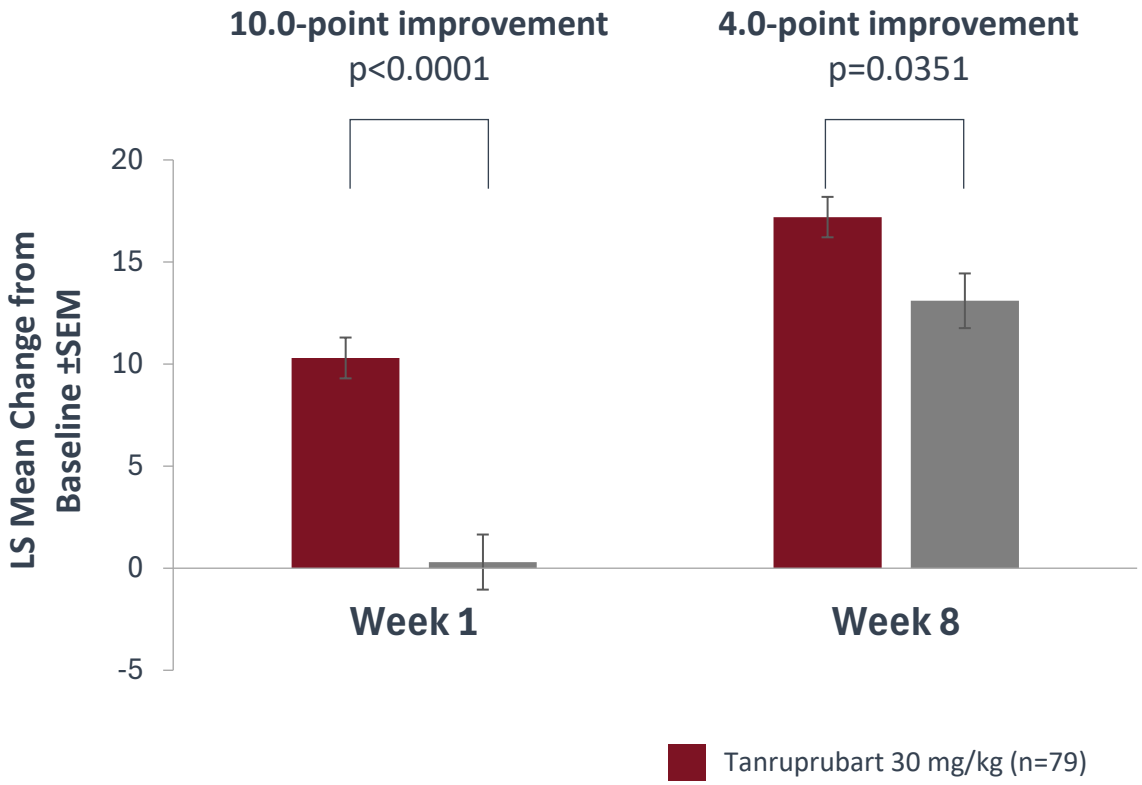
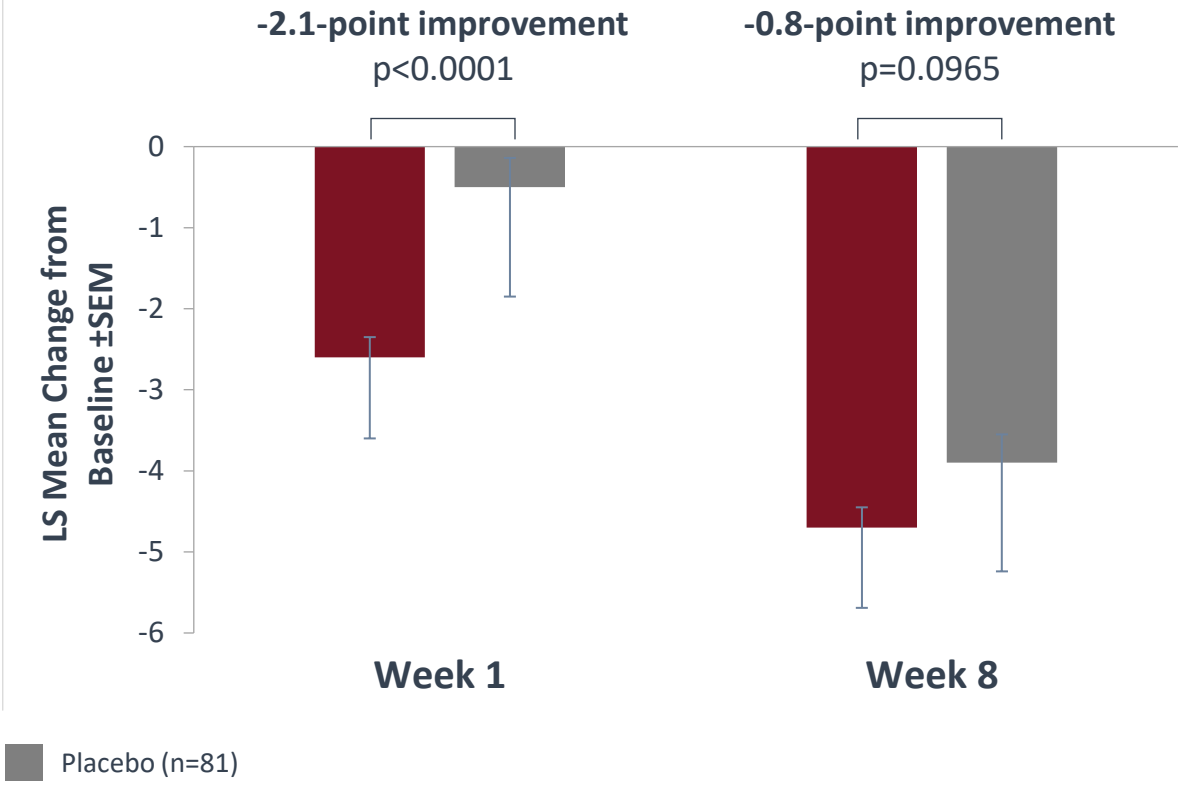
# Key Secondary Endpoints Demonstrated Treatment Benefit

## Improvement in Muscle Strength (MRCss)




## Reduced Motor Disability (ONLS)[1]




Tanruprubart 30 mg/kg (n=79)  Placebo (n=81)

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[1]ONLS - Overall Neuropathy Limitation Scale



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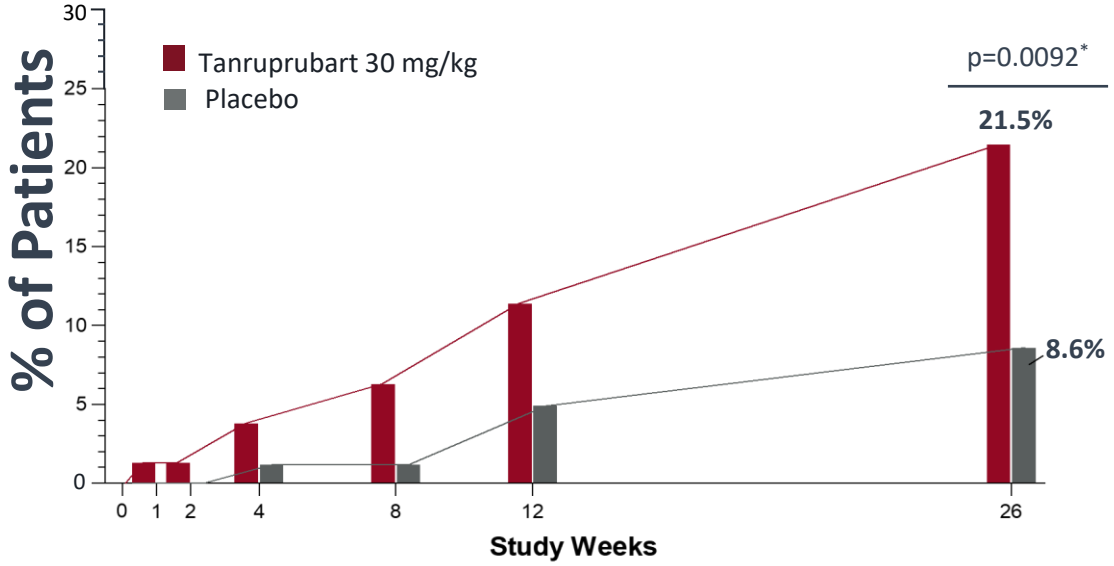
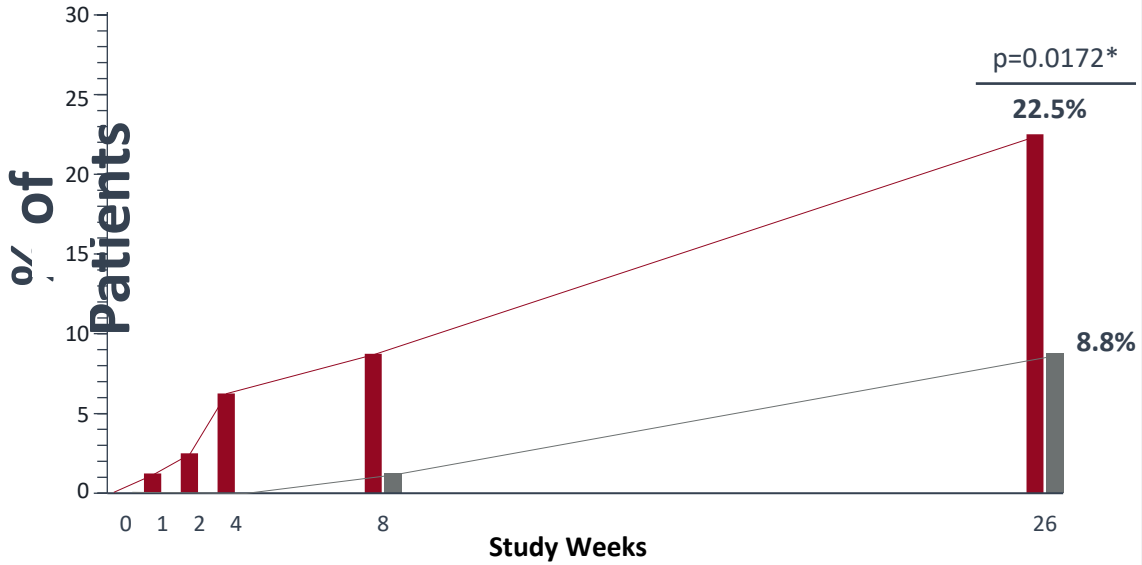
# Tanruprubart (ANX005) Treatment Effect is Durable Across Multiple Measures of Function and Mobility

## ~2X+ times more treated patients fully recover on multiple measures at week 26

### FULL RECOVERY
### GBS-DS=0




### NO LIMITATIONS
### ONLS (TOTAL SCORE=0)

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*Nominal

GBS-DS, Guillain-Barré syndrome Disability Score; ONLS, Overall Neuropathy Limitations Scale



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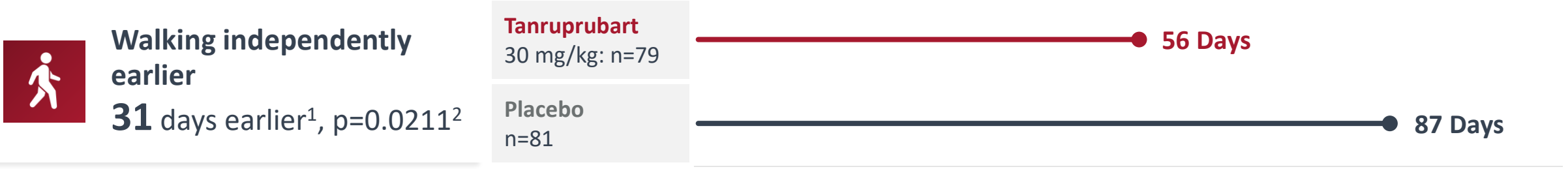
# Effect of Tanruprubart 30 mg/kg on Key Outcomes

## Helping Patients Achieve Their Independence Sooner

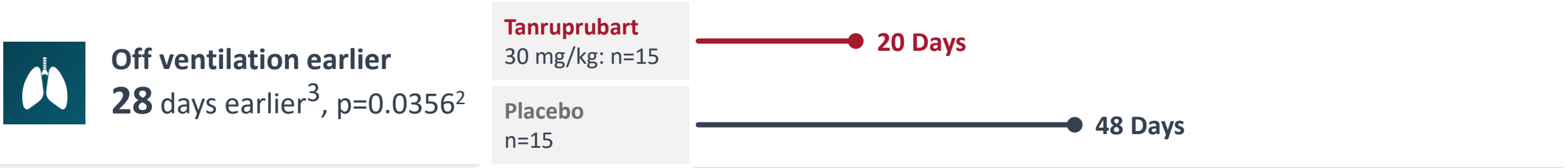
### Walking independently earlier

**31** days earlier[1], p=0.0211[2]




### Off ventilation earlier

**28** days earlier[3], p=0.0356[2]




### Fewer days in ICU

**7** fewer days[4], p=ns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ICU, intensive care unit; ns, not significant.
[1]Based on first scheduled visit of recording [2]Nominal [3]Among patients ventilated [4]Among patients requiring ICU



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# Tanruprubart (ANX005) Was Generally Well-Tolerated

## Majority of AES were mild (GRADE 1) to moderate (GRADE 2)

- Most common related events were infusion-related reactions
  - Majority were mild transient rashes
- SAEs and Grade 3 AEs balanced across groups, characteristic of disease morbidity

## 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 subjects reporting TEAEs, n (%)** | 79 (97.5) | 79 (100.0) | 80 (98.8) |
| **Number of subjects 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) |

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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; UTI, urinary tract infection.



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# Panel Discussion

**Jeff A. Allen, MD**

**Professor of Neurology**

University of Minnesota

**Avni Kapadia, MD**

**Assistant Professor of Neurology**

Baylor College of Medicine

**Nick Silvestri, MD, FAAN**

**Professor of Neurology, Associate Dean**

University at Buffalo





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# Thank You!