Indirect comparison of Nipocalimab Safety Versus FcRn Blockers, C5 Complement Inhibitors, Rituximab and IVIg in Generalized Myasthenia Gravis

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Background

- Generalized myasthenia gravis (gMG) is a rare, chronic autoimmune disease associated with fluctuating muscle weakness and significant morbidity.
- Multiple add-on therapies are used in gMG, including FcRn blockers, C5 complement inhibitors, and off-label therapies such as IVIg and rituximab; yet no head-to-head randomized comparisons are available.
- Nipocalimab demonstrated a favorable safety profile versus placebo + Standard of care (SOC) in the phase 3 VIVACITY-MG3 trial[1].
- Indirect treatment comparisons (ITCs) are required to assess comparative safety across available gMG therapies.

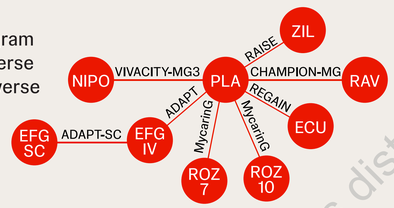
Objective

To assess the comparative safety of nipocalimab versus approved FcRn blockers, C5 complement inhibitors, and off-label therapies (IVIg and rituximab) in adults with AChR-positive generalized myasthenia gravis using indirect treatment comparisons.

Methods

A feasibility assessment was performed to inform methodological decisions. A Bayesian network meta-analysis (NMA) was conducted on the Acetylcholine Receptor-positive (AChR+) population, selected to ensure comparability across eligible trials. Model selection was based on best-fit criteria. Base-case analyses included eligible trials with similar follow-up duration and sensitivity analyses included all trials independent of trial duration. Results are reported as odds-ratio (OR) with 95% Credible intervals (CrI) and probability (P) of OR<1 favoring nipocalimab, interpreted according to Cope et al. 2013.[2]

FIGURE 1: A Network Diagram Representing the Any Adverse Event and Any Serious Adverse Event Networks in the AChR+ Population for FcRn inhibitors and C5 Complement Inhibitors.



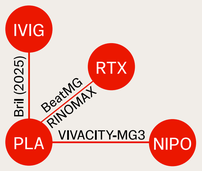


FIGURE 2: A Network Diagram Representing the AE and SAE Networks in the AChR+ Population for Off-label Treatments (IVIg and Rituximab)

Results

Safety outcomes assessed were:

- Any adverse event (AE)
- Any serious adverse event (SAE)

Comparisons were performed Bayesian network meta-analyses (NMAs).

Any adverse event (AE) Results

- The Bayesian NMA for AEs showed comparable results for nipocalimab versus other FcRn blockers and C5 inhibitors (P[OR<1]=16.7-83.8%) except for rozanolixizumab-10mg where nipocalimab was likely favorable (P[OR<1]=87.5%). **Figure 3**

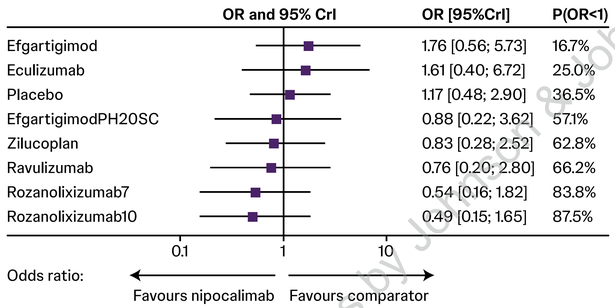


FIGURE 3: Odds Ratios (OR) and Bayesian probabilities for OR < 1 for nipocalimab versus FcRN blockers and C5 inihibitors for experiencing any AE

- The results vs IVIg and rituximab showed comparable AE profiles with probabilities of lower odds of any adverse events of 50.1% versus rituximab and 54.3% versus IVIg. **Figure 4**

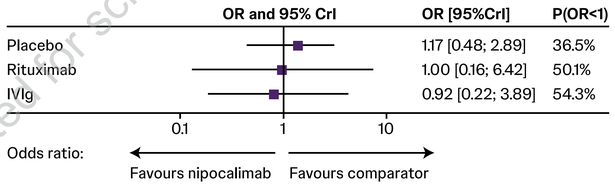


FIGURE 4: Odds Ratios (OR) and Bayesian probabilities for OR < 1 for nipocalimab versus IVIg and rituximab for experiencing any AE

Any Serious Adverse Event (SAE) Results

- For SAEs, nipocalimab results were comparable with eculizumab and efgartigimod (P[OR<1]=73.4%; 77.8%) and likely favorable versus other comparators (P[OR<1]=90.5% - 99.4%). **Figure 5**

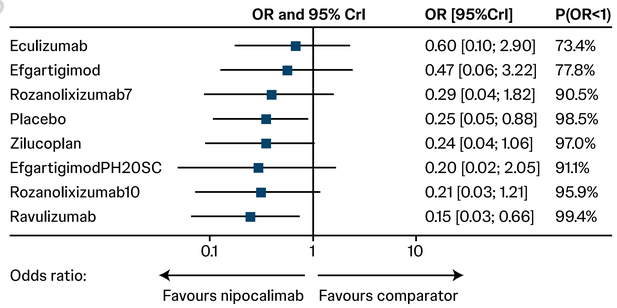


FIGURE 5: Odds Ratios (OR) and Bayesian probabilities for OR < 1 for nipocalimab versus FcRN blockers and C5 inihibitors for experiencing any SAE

- For SAEs, the results were favorable for nipocalimab compared with IVIg and rituximab, with probabilities of lower odds of any serious adverse events of 96.4% versus rituximab and 96.0% versus IVIg. **Figure 6**

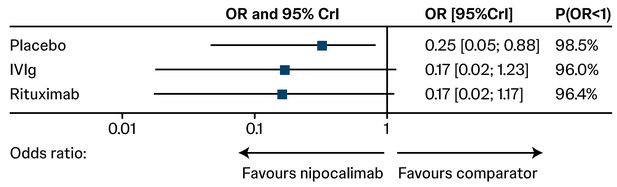


FIGURE 6: Odds Ratios (OR) and Bayesian probabilities for OR < 1 for nipocalimab versus IVIg and rituximab for experiencing any SAE

Key takeaway

- In the absence of head-to-head trials in generalized myasthenia gravis, indirect comparisons suggest that nipocalimab shows a comparable overall adverse event profile versus approved and off-label therapies, while serious adverse event outcomes consistently favor nipocalimab.

Conclusion

Nipocalimab demonstrated, **versus placebo**, a consistent safety profile with a favorable profile for serious adverse events.

Nipocalimab showed, **versus active comparators**, comparable rates of any adverse events, while serious adverse event outcomes consistently favored nipocalimab across analyses.

Overall, these findings support a **favorable benefit-risk profile** for nipocalimab within the gMG treatment landscape.

Limitations:

- The network of evidence is sparse, with most comparisons informed by a single clinical trial
- Heterogeneity in study populations and study designs may introduce bias

Presented at European Academy of Neurology (EAN), Geneva, Switzerland; June 27-30, 2026

Disclosures

Saiju Jacob has received research support/ honoraria or have been in the advisory board of Myaware, Alexion, Alnylam, Argenx, Eisai, Johnson and Johnson, Merck, Momenta, Novartis, Regeneron, Terumo BCT, UCB Pharmaceuticals and Amgen. This work was funded by Johnson & Johnson. Employees of Johnson & Johnson may hold stocks/stock options in Johnson & Johnson. Brian Hutton has previously received honoraria from Eversana Inc for methods advice related to systematic reviews and meta-analysis.

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1. Antozzi C, et al. Safety and efficacy of nipocalimab in adults with generalised myasthenia gravis (Vivacity-MG3): a phase 3, randomised, double-blind, placebo-controlled study. Lancet Neurol. 2025 Feb;24(2):105-116. doi: 10.1016/S1474-4422(24)00498-8. PMID: 39862879.
2. Cope S, et al. Quantitative summaries of treatment effect estimates obtained with network meta-analysis of survival curves to inform decision-making. BMC Med Res Methodol. 2013;13:147. doi:10.1186/1471-2288-13-147.

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