

immunopathological mechanism remains elusive, likely due to etiological heterogeneity among the variant presentations. This is best exemplified by the identification of nodal/paranodal antibodies, such as neurofascin 155, in a subgroup of CIPD patients who present with a distinct phenotype. **Methods:** We present the case of a 39-year-old male who presented with a 2-year history of progressive stocking-glove sensory loss and sensory ataxia. Electrophysiology confirmed an acquired demyelinating neuropathy, with serum anti-NF155 IgG4. His case was refractory to standard immunomodulatory therapy, including adequate trials of IVIG, steroids, azathioprine, and rituximab. He also had a non-therapeutic trial of PLEX, methotrexate, and tacrolimus. **Results:** After cessation of all immunomodulatory therapy for 2 years, he had spontaneous remission of his CIPD and near-complete resolution of electrophysiological/clinical abnormalities. **Conclusions:** This case provides insights into the natural history of NF155 “paranodalopathy” and highlights a unique case of supra-refractory CIPD which underwent spontaneous remission with near-complete resolution. Delayed effect from rituximab was posited as a contributor, however, the patient had no clinical or electrophysiological improvement 20-months after initiation of anti-CD20 therapy. Current data suggests the majority of CIPD patients respond to rituximab within 6-12 months.

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A phase 1, multicenter, randomized, placebo-controlled, multiple ascending dose study to evaluate the safety and tolerability of AMX0114 in ALS (LUMINA)

*S Paganoni (Boston) L Kett (Cambridge) R Bowser (Phoenix) L Kingston (Cambridge) E Mizerak (Cambridge) J Pesko (Cambridge) J Kerthi (Cambridge) J Timmons (Cambridge) A Genge (Montreal) S Blackmon (Cambridge)**

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Background: Axonal degeneration has been recognized as a key early contributor to the clinical presentation and pathogenesis of amyotrophic lateral sclerosis (ALS). Activation of the calcium-dependent cysteine protease calpain-2 is considered a critical effector of axonal degeneration. Based on evidence supporting a potential benefit of calpain-2 modulation in ALS and other neurodegenerative diseases, Amylyx developed AMX0114, an antisense oligonucleotide (ASO) inhibitor of calpain-2. This phase 1 study will assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of AMX0114 in people with ALS. **Methods:** LUMINA is planned to be conducted at ~15 sites in North America enrolling approximately 48 participants randomized 3:1 to receive AMX0114 or placebo. After study completion, an open-label extension study of AMX0114 will be implemented if data supports a positive benefit-risk profile. **Results:** The primary endpoints of the study include the incidence of adverse events (AEs), serious AEs, and dose-limiting toxicities. Secondary and tertiary endpoints include PK measurements (plasma and cerebrospinal fluid [CSF] levels of AMX0114), PD biomarkers, and functional measures of ALS progression. **Conclusions:** LUMINA is a first-in-human study evaluating the safety, tolerability, PK, and PD of AMX0114, the first ASO targeting calpain-2 in adult participants with ALS. Enrollment is planned to begin in Canada in early 2025.

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Final pooled analysis of efficacy and safety of rozanolixizumab cycles in patients with generalised myasthenia gravis: MycarinG and open-label extension studies

V Bril (Toronto) C Antozzi (Milan) A Druzd (Poznań) J Grosskreutz (Lübeck) AA Habib (Orange) S Sacconi (Nice) K Utsugisawa (Hanamaki) J Vissing (Copenhagen) T Vu (Tampa) F Grimson (Slough) B McDonough (Slough) I Pulido-Valdeolivas (Madrid) T Tarancón (Madrid)*

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Background: In the Phase 3 MycarinG study (MG0003/NCT03971422), one 6-week cycle of rozanolixizumab significantly improved myasthenia gravis (MG)-specific outcomes versus placebo. After MycarinG, patients could enrol in open-label extension studies (MG0004 then MG0007, or MG0007 directly). **Methods:** In MG0004 (NCT04124965), patients received once-weekly rozanolixizumab 7mg/kg or 10mg/kg for ≤52 weeks. In MG0007 (NCT04650854), after a cycle of rozanolixizumab 7mg/kg or 10mg/kg, subsequent cycles were based on symptom worsening at the investigator's discretion. Pooled data are reported across MycarinG, MG0004 (first 6 weeks) and MG0007 (final data) for patients receiving ≥2 symptom-driven cycles (efficacy; ≤13 cycles) or ≥1 cycle (safety). **Results:** 196 patients received ≥1 rozanolixizumab dose of whom 129 received ≥2 symptom-driven cycles (7mg/kg: n=70; 10mg/kg: n=59). Treatment response was maintained from Cycles 1–13: mean change from baseline to Day 43 in MG-Activities of Daily Living score ranged from -3.2 to -4.9 (7mg/kg) and -3.2 to -6.7 (10mg/kg). Quantitative MG and MG Composite scores also improved. Treatment-emergent adverse events (TEAEs) did not increase with repeated cyclic treatment, and most were mild/moderate; the most common event was headache. **Conclusions:** Rozanolixizumab showed consistent improvements across MG-specific outcomes up to 13 cycles and repeated cyclic treatment was generally well tolerated. Funding: UCB.

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Does single fiber EMG (SFEMG) pair number influence the outcome of patients initially referred for possible myasthenia gravis (MG)?

JD Kliot (Montreal) FG Moore (Montreal)**

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Background: Analysis of 20 pairs is the traditional standard when using SFEMG to diagnose MG. Some studies show that fewer pairs are needed if results are normal. We examined what impact this might have on long-term outcomes. **Methods:** Hospital charts of 239 consecutive patients who underwent SFEMG between January 2011, and July 18th, 2024, were reviewed. **Results:** 201 patients were identified; 128 had normal SFEMGs. Of the patients with normal SFEMGs, 58 (45.31%) had 12 pairs observed and 69 (53.91%) had 20 or more pairs observed. In the 12 pair group, 1 (1.72%) patient had delayed MG diagnosis, and 2 (3.45%) patients were referred for repeat SFEMGs; in the 20 or more group,

2 (2.90%) patients belong in each aforementioned category. No patients from either group were hospitalized for MG after SFMEG. Conclusions: Preliminary results demonstrate no difference in frequency of poor outcomes between patients who had 20 or more pairs observed and those who had 12 pairs observed, supporting the safety of shortening the test in appropriate situations.

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Post-hoc evaluation of the clinical effects of nipocalimab, a neonatal fragment crystallizable blocker, over time in the Vivacity MG3 study

R Nowak (New Haven) M Ait-Tihyaty (Titusville) I Turkoz (Titusville) K Gandhi (Titusville) R Rodriguez (Titusville) S Pease (Titusville) S Gingerich (Toronto) H Katzberg (Toronto)*

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Background: In generalized myasthenia gravis (gMG), there remains an unmet need for treatments providing meaningful symptom control. **Methods:** Mean changes in MG-ADL were compared between nipocalimab + standard-of-care (SoC) and placebo+SoC. The proportion of patients achieving: Minimal Symptom Expression (MSE), MG-ADL score 0/1, time with MSE, sustained within person meaningful change (WPMC) starting from Week 4, and time spent with WPMC were compared. **Results:** Nipocalimab+SoC demonstrated significant improvement in MG-ADL compared to placebo+SOC, LS-mean-change[SE] -4.7[0.329] vs -3.25[0.335]; Difference in means [SE]=-1.45 [0.470], $p=0.002$. The mean difference favoured nipocalimab+SoC, and was significant as early as week 1: LS-mean-change[SE]: -2.72[2.979] vs -1.77[2.426]; Difference in means[SE] -0.82[0.410], $p=0.046$. Nipocalimab+SoC patients were three times more likely to achieve MSE at any point during the study vs placebo; Odds Ratio[95% CI]: 3.0[1.3, 6.8]; 31.2% vs. 13.2%. For the 25 patients reaching MSE, the time sustaining MSE [percent time with MSE] was 101.5 days, (60.4%, nipocalimab+SOC) vs 55 days, (32.7%, placebo+SOC). Similarly, the proportion of patients with sustained WPMC favored nipocalimab+SOC, 55.8% vs 26.3%, placebo+SOC, $p<0.001$. The median percent time spent with WPMC was 84.5%, nipocalimab+SOC vs 39.9%, placebo+SOC, $p=0.007$. **Conclusions:** Based on MG-ADL data from Phase 3, nipocalimab an FcRn blocker, demonstrated rapid, substantial, and sustained symptom control.

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A randomized, open-label study on the effect of Nipocalimab on vaccine responses in healthy participants

M Cossu (Leiden) C Bobadilla Mendez (Spring House) A Jackson (La Jolla) E Myshkin (Cambridge) G Liu (Raritan) E Lam (Spring House) U Beier (Spring House) K Weisel (Spring House) B Scott (Spring House) M Ait-Tihyaty (Spring House) B Sattin (Toronto)* J Leu (Spring House) S Gao (Spring House) D Dimitrova (Spring House)

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Background: Nipocalimab is a human IgG1 monoclonal antibody targeting FcRn that selectively reduces IgG levels

without impacting antigen presentation, T- and B-cell functions. This study describes the effect of nipocalimab on vaccine response. **Methods:** Open-label, parallel, interventional study randomized participants 1:1 to receive intravenous 30mg/kg nipocalimab at Week0 and 15mg/kg at Week2 and Week4 (active) or no drug (control). On Day 3, participants received Tdap and PPSV[®]23 vaccinations and were followed through Wk16. **Results:** Twenty-nine participants completed the study and are included (active, $n=15$; control, $n=14$). Participants with a positive anti-tetanus IgG response was comparable between groups at Wk2 and Wk16, but lower at Wk4 (nipocalimab 3/15 [20%] vs control 7/14 [50%]; $P=0.089$). All maintained anti-tetanus IgG above the protective threshold (0.16IU/mL) through Wk16. While anti-pneumococcal-capsular-polysaccharide (PCP) IgG levels were lower during nipocalimab treatment, the percent increase from baseline at Wk2 and Wk16 was comparable between groups. Post-vaccination, anti-PCP IgG remained above 50mg/L and showed a 2-fold increase from baseline throughout the study in both groups. Nipocalimab co-administration with vaccines was safe and well-tolerated. **Conclusions:** These findings suggest that nipocalimab does not impact the development of an adequate IgG response to T-cell-dependent/independent vaccines and that nipocalimab-treated patients can follow recommended vaccination schedules.

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Miglustat: a first-in-class enzyme stabiliser for late-onset Pompe Disease

B Fox (Princeton)* T Mozaffar (Irvine) M Roberts (Salford) BJ Byrne (Gainesville) MM Dimachkie (Kansas City) RJ Hopkin (Cincinnati) PS Kishnani (Durham) B Schoser (Munich) AT van der Ploeg (Rotterdam) J Brudvig (Princeton) F Holdbrook (Princeton) V Jain (Princeton) F Johnson (Princeton) J Zhang (Princeton) G Parenti (Naples)

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Background: Late-onset Pompe disease (LOPD) is caused by a deficiency of acid α -glucosidase (GAA), leading to progressive muscle and respiratory decline. Cipaglucosidase alfa (cipa), a recombinant human GAA naturally enriched with bis-mannose-6-phosphate, exhibits improved muscle uptake but is limited by inactivation at near-neutral blood pH. Miglustat (mig), an enzyme stabiliser, binds competitively and reversibly to cipa, enhancing its stability and activity. **Methods:** In dose-finding studies, *Gaa*-/- mice were treated with cipa (20 mg/kg) +/- mig (10 mg/kg; equivalent human dose ~260 mg). Clinical study methodologies have been published (Schoser *et al. Lancet Neurol* 2021;20:1027–37; Schoser *et al. J Neurol* 2024;271:2810–23). **Results:** In *Gaa*-/- mice, cipa+mig improved muscle glycogen reduction more than cipa alone and grip strength to levels approaching wild-type mice. LOPD patients ($n=11$) treated with cipa alone showed dose-dependent decreases in hexose tetrasaccharide (Hex4) levels by ~15% from baseline, decreasing another ~10% with added mig (260 mg). In a head-to-head study, cipa+mig had a similar safety profile to α -glucosidase alfa. Among 151 patients (three trials), mig-related adverse events occurred in 21 (13.9%), none serious. **Conclusions:** Mig stabilised cipa in circulation, improving cipa exposure, further