reducing Hex4 levels and was well tolerated in clinical studies in patients with LOPD. Sponsored by Amicus Therapeutics, Inc.

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Clinical predictors of disease progression and survival in ALS: insights from the Canadian Neuromuscular Disease Registry

D Daudu (London) J Arocha Perez (London)* K Henley (Calgary) V Hodgkinson (Calgary) A Abrahao (Toronto) H Briemberg (Vancouver) M Chum (Hamilton) A Genge (Montreal) A Marrero (Moncton) S Kalra (Edmonton) W Johnston (Edmonton) R Massie (Montreal) G Matte (Montreal) M Melanson (Kingston) C O'Connell (Halifax) K Schellenberg (Saskatoon) S Taylor (Halifax) L Zinman (Toronto) Canadian Neuromuscular Disease Registry L Korngut (Calgary) C Shoesmith (London)*

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Background: Amyotrophic Lateral Sclerosis (ALS) leads to progressive functional decline and reduced survival. Identifying clinical predictors like ALSFRS-R and FVC is essential for prognosis and disease management. Understanding progression profiles based on diagnostic characteristics supports clinical trial design and assessment of treatment response. This study evaluates disease progression and survival predictors in ALS patients from the CNDR. Methods: 1565 ALS patients in the CNDR were analyzed to assess baseline ALSFRS-R, FVC, time from symptom onset to diagnosis, and their association with disease progression and survival. Results: At diagnosis, ALSFRS-R was 44.7 (SD = 5.46), with 72.3% scoring ≥44. Mean FVC was 84.2% (SD = 23.3), with 78.3% of patients having FVC ≥65%. ALSFRS-R declined at 1.06 points/month (SD = 1.33), with faster progression in patients diagnosed within 24 months (1.61 points/month). Patients with ALSFRS-R ≥44 had a median survival of 41.8 months, compared to 30.9 months for those <44 ($p < 0.001$). Similarly, FVC ≥65% was associated with longer survival (35.4 vs. 29.5 months, $p = 0.002$). Conclusions: ALSFRS-R and FVC at diagnosis predict survival and inform clinical decision-making. These findings highlight the importance of early diagnosis and targeted interventions to slow disease progression and improve patient outcomes.

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Effectiveness and safety of ravulizumab in generalized Myasthenia Gravis (gMG): Updated analysis from a global registry

*P Narayanaswami (Boston) MT Pulley (Jacksonville) SP Macwan (Rancho Mirage) JM Winkley (Lexington) L Zeinali (Mississauga) C Liu (Baar) V Juel (Durham) R Tandan (Burlington) F Saccà (Napoli) AJ Gordon (Lake Barrington) A Yegin (Boston) JF Howard, Jr. (Chapel Hill) M Nicolle (London)**

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Background: The complement C5 inhibitor (C5IT), ravulizumab, is approved in Canada for the treatment of anti-acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gMG). Updated effectiveness and safety results from the ongoing MG SPOTLIGHT Registry (NCT04202341) are reported. Methods: MGFA classification and MG-ADL total scores were assessed in patients who received ravulizumab only (ravu-only) or transitioned from eculizumab to ravulizumab (ecu-to-ravu), with data available prior to C5IT initiation ("pre-C5IT") and ≥1 assessment post-initiation ("post-ravu"). Results: Of 52 patients with 2 post-ravu assessments, average treatment duration was 10.4 months at last assessment (LA). Mean±SD MG-ADL scores improved (pre-C5IT: 7.6±3.6; LA: 3.4±3.3), as did the proportions of patients with minimal symptom expression (MSE, MG-ADL≤1) (pre-C5IT: 1/52 [2%]; LA: 17/52 [33%]) and MGFA classification 0-II (pre-C5IT: 18/45 [40%]; LA: 40/45 [89%]). In the ravu-only subgroup, outcomes improved (pre-C5IT vs LA): MG-ADL, 6.3 ±3.0 vs 4.0±3.4; MGFA 0-II, 9/14 [64%] vs 12/14 [86%]. The ecu-to-ravu subgroup sustained continued gradual improvement from last eculizumab assessment to LA: MG-ADL, 4.4±4.2 vs 3.0±2.8; MGFA 0-II, 19/21 [90%] vs 20/21 [95%]. Ravulizumab was well tolerated; no meningococcal infections were reported. Conclusions: These results demonstrate the long-term effectiveness and safety of ravulizumab in routine clinical practice in patients with gMG.

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A portrait of generalized Myasthenia Gravis in Canada: analysis of the Adelphi MG II disease specific programme

O Blanchard (Montreal) K Quansah (Toronto) AE Batista (Titusville) A Erman (Toronto) H Connolly (Bollington) ZA Siddiqi (Edmonton)*

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Background: Generalized myasthenia gravis (gMG) is a rare, chronic, autoimmune disease characterized by muscle weakness and fatigue. This study aims to describe the natural history, disease burden and treatment patterns of gMG patients in Canada. Methods: Data was analyzed from the Adelphi MG II DSP™, a gMG patient-level cross-sectional database, collected through surveys between February-June 2024. Neurologists provided sociodemographic, symptomatology, and treatments data. Results: Fifteen neurologists provided data for 46 gMG patients. The cohort's mean (SD) age was 58.1 (14.7) years, 52.2% male, 82.6% White/Caucasian and 89.1% were anti-AChR Ab positive. Mean time since diagnosis was 3.4 (3.1) years, 22% reported a change in employment status due to gMG. Most had public insurance (68.9%). Disease severity was mostly MGFA class II (78.2%) patients. Common symptoms included eyelid ptosis (76.1%), dysarthria (50.0%), and dyspnea (54.3%) – mean MG-ADL was 5.6 (5.1). During their disease course, 34.9% experienced ≥1 myasthenic crisis, while 25.6% reported symptom exacerbation. At time of survey, patients had used 1.8 (0.9) lines of maintenance treatment. Most prescribed treatments (alone or in combinations) were pyridostigmine (95.6%), corticosteroids (48.9%), non-steroidal immunosuppressants (42.2%), Immunoglobulins (31.1%), and biologics (22.2%). Conclusions: gMG patients continue to experience symptoms burden and crisis/exacerbations. These findings highlight an unmet need for

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new, safe and effective therapeutics that are publicly covered to manage gMG-related clinical manifestations.

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Therapeutic options for changing the course of disease in generalized myasthenia gravis (gMG) and fiscal consequences for Canadian governments

H Katzberg (Toronto) C Qi (Boston) A Paquete (Lisbon) S Raza (Ghent) C Kassardjian (Toronto) Z Siddiqi (Edmonton) M Connolly (Lisbon) N Kotsopoulos (Lisbon) R Kaprielian (Vaughan) J Locklin (Vaughan) G Phillips (Boston)*

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Background: Generalized myasthenia gravis (gMG) is a potentially life threatening chronic autoimmune disease that can impair patients' ability to work effectively and increase reliance on public support benefits. A public economic framework was used to explore how treatment influences patients' and caregivers' economic activity, including tax revenues and public support in Canada. Methods: Natural history of gMG was simulated using a multi-state Markov cohort model. Health states were based on MG Activities of Daily Living (MG-ADL) total score in patients with AChR-Ab+ refractory gMG. Treatment, costs, and economic outcomes of patients taking efgartigimod were compared with alternative therapeutic options. Canadian public support benefits were based on official government sources. Results: Improved MG-ADL states predict higher workforce participation, lower rates of disability and less caregiving needs, resulting in higher tax revenues and less public support costs. Compared to alternative therapeutic options, efgartigimod is estimated to yield lifetime fiscal gains of $458,755 that exceed the incremental cost of $291,073, suggesting the Canadian government receives $1.6 for every $1.0 spent on efgartigimod for the treatment of gMG. Conclusions: Compared with alternative options, efgartigimod generated a positive fiscal return for the Canadian governments with additional savings from disease management, public benefits, and averted tax revenue losses.

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Investigating the bioequivalence, injection speed, and usability of subcutaneous efgartigimod PH20 administration using a prefilled syringe

B Mwaikambo (Ghent) F Borgions (Ghent) K Allosery (Ghent) J Noukens (Liempde) C De Muynck (Ghent)*

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Background: Efgartigimod, a human immunoglobulin G1 (IgG1) antibody Fc fragment, reduces IgG levels through neonatal Fc receptor blockade. Efgartigimod PH20 SC (1000-mg fixed dose, coformulated with recombinant human hyaluronidase PH20) is provided in a vial administered via a separate syringe (V+S). Here, we investigate bioequivalence, safety, and tolerability of efgartigimod PH20 SC administered via prefilled syringe (PFS) vs V+S in healthy participants. Methods: Bioequivalence was assessed in a phase 1, open-label study. Healthy participants (n=72) were randomized to receive one injection of efgartigimod PH20 SC via PFS or V+S in a crossover design. Separate studies evaluated feasibility of different injection speeds and usability of the PFS. Results: Bioequivalence between efgartigimod PH20 SC via PFS or V+S was established, as the 90% CI around the geometric least-squares mean ratio of C_{max} and $AUC_{0\text{-}inf}$ was within predefined criteria (80.00%-125.00%). Most adverse events were mild to moderate. No observed differences in incidence of reported injection site reactions emerged. No serious adverse events or deaths occurred. Rapid (20-second) administration was feasible and the PFS could be safely prepared and administered by participants/caregivers. Conclusions: Efgartigimod PH20 SC administered via PFS is bioequivalent to efgartigimod PH20 SC administered via V+S, which may provide an additional convenient treatment option.

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Early and sustained response over time with zilucoplan in generalised Myasthenia Gravis: 120-week post hoc analysis of RAISE-XT

O Blanchard (Montreal) S Bresch (Nice) M Freimer (Columbus) C Hewamadduma (Sheffield) M Leite (Oxford) A Maniaol (Oslo) K Utsugisawa (Hanamaki) R Beau Lejdstrom (Bulle) B Boroojerdi (Monheim) F Grimson (Slough) N Savic (Bulle) JF Howard (Chapel Hill)*

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Background: RAISE-XT (NCT04225871; Phase 3 study) showed clinically meaningful and sustained improvements in myasthenia gravis (MG)-specific outcomes with zilucoplan, a macrocyclic peptide complement component 5 inhibitor, in patients with acetylcholine receptor autoantibody-positive generalised MG. Methods: Adults self-administered once-daily subcutaneous zilucoplan 0.3mg/kg. This *post hoc* analysis assessed durability of response to Week 120 in MG-Activities of Daily Living (MG-ADL) and Quantitative MG (QMG) responders at Week 1 of two double-blind studies (NCT03315130, NCT04115293). Responder definitions: improvements of ≥3-points (MG-ADL) or ≥5-points (QMG) (interim data cut: 11 November 2023). Results: 93 patients were randomised to zilucoplan 0.3mg/kg in the double-blind studies; 43.0% (n=40/93) and 33.3% (n=31/93) were MG-ADL and QMG responders, respectively, at Week 1. Week 1 responders spent a median (range) of 98.9% (5.8–99.2) and 99.0% (2.5–99.2) time in response up to Week 120 for MG-ADL and QMG. Week 1 non-responders spent a median (range) of 84.6% (0.0–98.3) and 66.7% (0.0–98.9) time in response up to Week 120 for MG-ADL and QMG, with most responding later in the study. Conclusions: Among early (Week 1) zilucoplan responders, time in response remained high (99%) up to Week 120. These data demonstrate rapid and sustained efficacy with long-term zilucoplan treatment.

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