Activities of Daily Living score of 0 or 1) were estimated for efgartigimod (EFG), intravenous immunoglobulin (IVIg), and eculizumab (ECU). All treatments were used in conjunction with CT. Costs per improved outcome (CPR) were compared between EFG, IVIg, and ECU. Efficacy evaluated at week 4 of respective phase 3 randomized trials (ADAPT [NCT03669588], NCT02473952, REGAIN [NCT01997229]. Annual drug acquisition and administration costs (2021 USD) were considered.

Results

Compared with CT, mean NNTs to achieve one point improvement and MCID in QMG were 0.19 and 2.03 for EFG, 0.52 and 7.14 for IVIg, and 0.56 and 6.25 for ECU. NNTs to achieve an additional patient with MSE was 3.46 for EFG and 8.13 for ECU. Compared to EFG, the mean annual CPR to achieve one point improvement and MCID in QMG were higher for IVIg (Difference [95% confidence interval] = $36,130 [$14,024, $58,237] per point improvement in QMG; $661,561 [$0, $1,546,275] per one patient with MCID in QMG) and ECU ($340,659 [$158,038, $523,280]; $3,838,718 [$1,470,740, $6,206,695]). Cost to achieve one additional patient with MSE was $4,761,649 [$2,859,671, $6,663,626] higher for ECU compared with EFG.

Conclusions

Evidence indicates more favorable treatment benefit and economic value for EFG with fewer NNT and lower cost required to achieve improved outcomes compared to other treatments.

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The ExTINGUISH Trial: A Phase-2B Randomized Placebo-Controlled Trial of Inebilizumab in Anti-NMDA Receptor Encephalitis

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Objective

To assess the safety and efficacy of inebilizumab in patients with anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis.

Background

The lack of approved therapies for NMDAR encephalitis has led to substantial variability in treatment. High-quality data is needed to guide treatment and optimize long-term outcomes in recovering patients. Inebilizumab is a humanized anti-CD19 monoclonal antibody that can be administered intravenously with good CSF penetration and high target engagement. Inebilizumab may be an efficacious treatment for NMDAR encephalitis, with the potential to achieve early robust and sustained suppression of NMDAR autoantibodies and CD19+ plasmablasts and plasma cells leading to better long-term outcomes.

Design/Methods

The ExTINGUISH trial is a Phase 2B randomized double-blind placebo-controlled trial designed to evaluate the safety and efficacy of inebilizumab 300 mg for the acute treatment of moderate-to-severe NMDAR encephalitis. 120 participants will be enrolled at 20 US and two European sites (Barcelona, Spain; Rotterdam, The Netherlands). All patients will receive standard "first-line" immunotherapies prior to randomization. Cyclophosphamide IV rescue therapy will be provided after 6 weeks to patients who fail to respond to initial treatment. Motor, cognitive, and functional outcomes will be assessed over 96 weeks. Study operations will be supported via the NINDS-supported NeuroNEXT infrastructure.

Results

Primary outcomes will be ascertained at 16 weeks using the change in modified Rankin scale (adjusted for rescue therapy) and accepted safety measures. Comprehensive neuropsychological tests, bedside cognitive screening tools, and quality of life/ functional indices will be measured across study participation (secondary outcomes). Clinical data will be combined with biofluid biomarkers of immune activation to inform the biologic contributors to outcomes and identify surrogate endpoints that may be used in future clinical trials (tertiary outcomes).

Conclusions

ExTINGUISH Trial findings will immediately influence patient care, while informing the design and implementation of future clinical trials in autoimmune encephalitis.

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Safety, Efficacy, And Pharmacokinetics of Argx-117 in Adults With Multifocal Motor Neuropathy: A Global, Multicenter, Placebo Controlled Phase 2 Study (Arda)

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Objective

To report the study design of a Phase 2, multicenter, randomized, placebo controlled, parallel-group study (ARDA, NCT05225675) will assess the safety, efficacy, PK, and PD of ARGX-117 in adults with MMN.

Background

Multifocal motor neuropathy (MMN) is a chronic, immune-mediated neuropathy characterized by progressive asymmetric weakness predominantly affecting the distal upper limbs. MMN is often associated with anti-GM1 IgM antibodies targeting the axolemma at the node of Ranvier, leading to activation of the classical complement pathway which drives subsequent damage to the axon. IVIg is the only proven effective therapy. ARGX-117 is a novel monoclonal antibody that inhibits complement factor 2 (C2). Using an in vitro model for MMN, ARGX-117 was shown to block IgM-mediated classical pathway complement activation on both motor neurons and Schwann cells. ARGX-117 is being studied in adults with MMN in a Phase 2, multicenter, randomized, placebo controlled, parallel-group study.

Design/Methods

Forty-eight participants will be recruited and assigned to one of two dosing cohorts (24 participants each) and randomized 2:1 within each cohort to receive either ARGX-117 or placebo. Key inclusion criteria include: diagnosis of probable or definite MMN per 2010 EFNS/PNS guidelines, stable IVIg regimen, and IVIg treatment dependency. The primary objective is safety based on adverse event monitoring and other safety assessments. Secondary objectives include assessment of efficacy measured as strength and functional disability, pharmacokinetics, pharmacodynamics (C2 and CH50), and immunogenicity of ARGX-117. After completing the 16-week treatment period, participants may enroll in an open-label extension study, or enter the safety follow-up period.

Results

This ongoing phase 2 study will assess the safety and efficacy of ARGX-117 in participants with MMN.

Conclusions

The results of this study will inform and direct future studies of ARGX-117 in this patient population.

Disclosure: Dr. Allen has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Argenyx. Dr. Allen has received personal compensation in the range of $500-$4,999 for serving as a Consultant for csl behring. Dr. Allen has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Takeda. Dr. Allen has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Grifols. Dr. Allen has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Argenx. Dr. Allen has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for grifols. Dr. Allen has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Allen has received personal compensation in the range of $10,000-$49,999 for serving on a Speakers Bureau for CSL behring. Dr. Nobile-Orazio has received personal compensation in the range of $500-$4,999