study); EMD Serono, Genentech/Roche (contracted research); Genentech/Roche (scientific advisory board for OBOE study); Novartis (scientific advisory board for ASCLEPIOS I and II); Projects in Knowledge (CE provider) (preparation of educational manuscripts, activities).

KEYWORDS: Disease-modifying treatments in MS, Immunology and MS, Infection risk

(DMT12) Evaluating Humoral Immune Response to mRNA COVID-19 Vaccines in Siponimod-Treated Patients With Advancing Forms of RMS: A COVID-19 Vaccine Substudy of the EXCHANGE Trial

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BACKGROUND: Siponimod is approved in the United States for treatment of adults with relapsing multiple sclerosis (RMS). Given the ongoing COVID-19 global pandemic, it is important to assess whether patients can mount an antiviral humoral immune response to COVID-19 vaccines while receiving siponimod. **OBJECTIVES:** To assess humoral immune response to nonlive COVID-19 mRNA vaccines (Pfizer/Moderna) in a subset of patients enrolled in EXCHANGE (trial registration: NCT03623243), a 6-month, open-label, single-arm phase 3b trial of conversion to siponimod in patients with advancing forms of RMS. **METHODS:** This is a single-arm pilot substudy in siponimod-treated patients currently participating in the core EXCHANGE study who have received a full course (2 doses) of mRNA COVID-19 vaccine. Patients enrolled in EXCHANGE were aged 18 to 65 years with advancing forms of RMS, with Expanded Disability Status Scale scores of 2.0 to 6.5, and taking continuous oral/injectable/infusion disease-modifying therapies for at least 3 months at the time of consent. Patients with a known previous COVID-19 diagnosis will be excluded from the substudy, and evaluation of immunoglobulin G (IgG) response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleocapsid protein will be assessed on study. Patients in the substudy will continue taking siponimod as per the EXCHANGE study protocol. The substudy will evaluate the number of patients achieving a positive IgG response to SARS-CoV-2 spike protein 14 days or more after full-course vaccination. Exploratory end points include rate of seroconversion and evaluation of the magnitude of the humoral response to COVID-19 vaccination. **RESULTS:** This substudy plans to enroll up to 20 patients from the EXCHANGE core study. An interim analysis will be performed after collection of substudy assessments. The following data will be presented together with the detailed substudy design: substudy patient demographic characteristics, including MS history, number of patients achieving vaccination response via the presence of serum SARS-CoV-2 spike IgG antibodies, and quantitative humoral response to COVID-19 vaccine. **CONCLUSIONS:** This substudy will contribute to a better understanding of humoral immune responses that occur in siponimod-treated patients with advancing forms of RMS after COVID-19 mRNA vaccination.

DISCLOSURES: *Amit Bar-Or: Accure, Atara Biotherapeutics, Biogen, Bristol Myers Squibb/Celgene/Receptos, GlaxoSmithKline, Gossamer, Janssen/Actelion, Medimmune, Merck/EMD Serono, Novartis, Genentech/Roche, Sanofi Genzyme (consulting fee, participated as a speaker in meetings sponsored by); Biogen Idec, Genentech/Roche, Merck/EMD Serono, Novartis (grant support to the University of Pennsylvania). Yang Mao-Draayer: Acorda, Biogen, Bayer Pharmaceutical, Bristol Myers Squibb/Celgene, EMD Serono, Genentech/Roche, Janssen, Teva (consulting fee); Chugai, Genentech/Roche, National Institutes of Health National Institute of Neurological Disorders and Stroke R01-NS080821, National Institute of Allergy and Infectious Diseases Autoimmune Center of Excellence UM1-AI110557, UM1 AI144298-01, Patient-Centered Outcomes Research Institute (contracted research); Novartis, Sanofi Genzyme (consulting fee, contracted research). Silvia R. Delgado: Mapi Pharma (contracted research); Novartis (consulting fee, contracted research). Robert J. Fox: Actelion, Celgene, EMD Serono, Genentech, Immunic, Teva (consulting fee); Biogen (consulting fee, contracted research); Novartis (consulting fee, contracted research, grants). Linda-Ali Cruz, Xiangyi Meng, Gina Mavrikis Cox: Novartis (employee). Stanley L. Cohan: AbbVie, Adamas, Alithios, Biogen, EMD Serono, Genentech/Roche, MedDay, Novartis, Sanofi Genzyme (contracted research); Biogen, Celgene, Genentech/Roche, Novartis, Pear Therapeutics, Sage Therapeutics, Sanofi Genzyme (consulting fee); Biogen, Genentech/Roche, Sanofi Genzyme (speakers' bureau).*

KEYWORDS: COVID-19 vaccination, Disease-modifying treatments in MS

(DMT13) Early Clinical Experience With Cladribine Tablets in a Real-World Aging Population

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BACKGROUND: Cladribine, a deoxyadenosine analogue, transiently and preferentially depletes B and T lymphocytes, disrupting the central immune cascade in multiple sclerosis (MS). Cladribine tablets are an oral, short-course (four 4-day to-5-day courses over 2 years) disease-modifying therapy (DMT) indicated for the treatment of relapsing forms of MS. The efficacy and safety of cladribine tablets was demonstrated in clinical trials, including the phase 3 CLARITY trial and its extension; however, the real-world clinical experience is still emerging. An area of growing interest is the use of DMTs in patients with advanced age. Understanding the risk/benefit profile of using a noncontinuous immunosuppressive DMT in this population is of extreme importance given immunosenescence and the increasing comorbidities with age. **OBJECTIVES:** To report our early experience using cladribine tablets in a real-world US cohort of patients with MS, many with advanced age. Outcomes presented include patient characteristics at treatment initiation, previous DMT use, safety, and lymphocyte counts. **RESULTS:** We report on 77 patients who initiated therapy with cladribine tablets by the data cutoff date (June 2021). Median age at cladribine tablet initiation was 46 years (range, 24-71 years), and 40% of patients were 50 years or older at initiation. Median disease duration was 13 years (range, 2-34 years), and median baseline Expanded Disability Status Scale score was 4 (range, 0-7.5). The mean number of previous DMTs was 2.5; only 4% of patients were treatment naïve. Mean follow-up was 365 days, and 31% of patients completed both treatment courses by the data cutoff date. Overall, cladribine tablets were well tolerated. Thirty-four percent of patients experienced lymphopenia, with no patients experiencing grade 3 or 4 lymphopenia. No adverse events occurred in 3% or more of patients. Updated data, including preliminary efficacy data, will be presented in the poster. **CONCLUSIONS:** In this cohort of patients initiating cladribine tablets in the real-world setting, the initial treatment was well tolerated, even among those with advanced age. There were no new safety signals. The adverse effect profile was consistent with that seen in the clinical trial program, even in an aging patient population in which comorbid conditions and immunosenescence may increase. Owing to the short follow-up time, it was not possible to assess long-term outcomes. Ongoing follow-up will further expand on these results as more patients complete their full treatment course.

DISCLOSURES: *Deborah Chandler, Amparo Gutierrez: Orlando Health (speakers' bureau).*

KEYWORDS: Disease-modifying treatments in MS

(DMT14) Long-term Efficacy and Safety, Including COVID-19 Outcomes, Among Ozanimod-Treated Patients With Relapsing Multiple Sclerosis in the DAYBREAK Open-Label Extension Trial

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