26th Annual Meeting of the European Charcot Foundation

Baveno, Italy 15–17 November 2018

Presentation preference: Oral or Poster

Title: Updated safety analysis of Cladribine Tablets (CT) in the treatment of patients with multiple sclerosis (MS)

Short Title: Updated safety analysis of Cladribine Tablets

Main author: S. Cook[1]

Additional authors: G. Giovannoni[2], T. Leist[3], S. Syed[4], A. Nolting[5], R. Schick[5]

[1]Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, NJ, United States; [2]Queen Mary University of London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK; [3] Jefferson University, Comprehensive MS Centre, Philadelphia, United States; [4]EMD Serono Research & Development Institute Inc., Billerica, MA, United States; [5]Merck KGaA, Darmstadt, Germany.

Introduction: Integrated analysis of pooled long-term safety data allowed comprehensive characterisation of the CT safety profile in patients with relapsing MS (RMS). Previous characterisation of a monotherapy oral cohort treated with CT 3.5 mg/kg (CT3.5) included cumulative safety data to Feb 2015, >3 years beyond last clinical study completion.

Objective: Two-year update of the serious treatment emergent adverse event (TEAE) profile from the CT3.5 integrated safety analysis.

Methods: The monotherapy oral cohort was derived from CLARITY, CLARITY Extension, and ORACLE-MS trials, and the PREMIERE registry. 923 patients received CT3.5; 641 patients received placebo. Adjusted AE incidences per 100 patient-years (Adj-AE per 100PY) were calculated. Data cut-offs were cumulative to Feb-2015 (previously presented, “Period-1”) and cumulative to May-2017 (updated, “Period-2”). Serious adverse drug reactions (ADR; implied causality) from post-marketing sources are summarised.

Results: Demographics at respective study enrolment, including age (36.5years, CT3.5), proportion of females (66.3%, CT3.5) and prior disease modifying drug experience, were balanced among treatment groups. Respective rates of Adj-AE per 100PY were (presented as CT3.5, placebo): ≥1 serious TEAE: 3.88, 3.24 (Period-2) and 4.00, 3.57 (Period-1); serious lymphopenia (preferred term

[PT]) 0.11, 0 (Period-2) and 0.12, 0 (Period-1); serious infection and infestations (system organ class [SOC]): 0.63, 0.44 (Period-2) and 0.69, 0.50 (Period-1); for serious herpes zoster (PT): 0.05, 0 (Period-2) and 0.06, 0 (Period-1); serious neoplasms, benign, malignant and unspecified (SOC) 0.65, 0.35 (Period-2) and 0.74, 0.50 (Period-1). Regarding post-marketing data, 11 serious ADRs were reported; none are new safety findings for CT3.5.

Conclusions: This integrated analysis confirms the serious TEAE profile associated with CT3.5 treatment of patients with early and active RMS. The updated profile (Period-2) was generally consistent with that from 2-years prior (Period-1). No new major safety findings were identified in the updated dataset, where patients were followed for ≤10-years.

The CLARITY study: NCT00213135; The CLARITY Extension study: NCT00641537; The ORACLE-MS study: NCT00725985; The PREMIERE registry: NCT01013350

Disclosures: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

Author disclosures

SC has received honoraria for lectures/consultations from Merck, Bayer HealthCare, Sanofi-Aventis, Neurology Reviews, Biogen Idec, Teva Pharmaceuticals, and Actinobac Biomed Inc.; has served on advisory boards for Bayer HealthCare, Merck, Actinobac Biomed Inc., Teva Pharmaceuticals, and Biogen Idec; and received grant support from Bayer HealthCare.

GG has received speaker honoraria and consulting fees from Abbvie, Actelion, Atara Bio, Almirall, Bayer Schering Pharma, Biogen Idec, FivePrime, GlaxoSmithKline, GW Pharma, Merck, Pfizer Inc, Protein Discovery Laboratories, Teva Pharmaceutical Industries Ltd, Sanofi-Genzyme, UCB, Vertex Pharmaceuticals, Ironwood, and Novartis; and has received research support unrelated to this study from Biogen Idec, Merck, Novartis, and Ironwood.

TL has received consultancy fees or clinical research grants from Acorda, Bayer, Biogen, Daiichi, EMD Serono, Novartis, ONO, Pfizer, Teva Neuroscience.

SS is an employee of EMD Serono Research and Development Institute Inc., a business of Merck KGaA, Darmstadt, Germany.

AN and **RS** are employees of Merck KGaA, Darmstadt, Germany.