

Full title: Innate Immune Cell Counts in Patients with Relapsing-Remitting Multiple Sclerosis (RRMS) Treated with Cladribine Tablets 3.5 mg/kg in CLARITY/CLARITY Extension

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Background: Lymphopenia was the most common adverse event in CLARITY/CLARITY Extension. Absolute lymphocyte counts (ALC) recovered towards the normal range over time.

Objective: To evaluate the effect of cladribine tablets (CT) on innate immune cell counts.

Methods: Pooled data from patients (N=685) randomised to CT3.5mg/kg (CT3.5) in CLARITY/CLARITY Extension, and data from patients (N=435) randomised to placebo (PBO) in CLARITY and followed up in PREMIERE were evaluated.

Results: At baseline (start of CLARITY or CLARITY Extension), median (Q1–Q3) neutrophil counts were CT3.5=4.19×10⁹/L (3.30–5.31) and PBO=4.20×10⁹/L (3.41–5.35). At the end of Year 1 (48 weeks), median neutrophil counts were CT3.5=3.80×10⁹/L (2.91–4.94) and PBO=4.24×10⁹/L (3.28–5.50). At the end of Year 2 (96 weeks), neutrophil counts were CT3.5=3.71×10⁹/L (2.90–4.70) and PBO=4.30×10⁹/L (3.32–5.46). At the end of Years 3 and 4 (144 and 192 weeks; no further treatment), CT3.5 neutrophils plateaued at 3.60×10⁹/L. PBO median neutrophils were 4.28×10⁹/L (3.30–5.25) and 3.46×10⁹/L (2.49–5.80) at these timepoints. Following CT3.5 treatment, neutrophil counts remained within the normal range (>2.03×10⁹/L) over the 2 treatment years and beyond, and ≤6 (<2%) patients treated with CT 3.5 reported Common Terminology Criteria for Adverse Events v3.0 Grade 3 or 4 neutropenia at any single time point.

Baseline median (Q1–Q3) monocyte counts were CT3.5=0.40×10⁹/L (0.30–0.50) and PBO=0.42×10⁹/L (0.31–0.53). At the end of Year 1, the monocyte counts were CT3.5=0.36×10⁹/L (0.27–0.45) and PBO=0.42×10⁹/L (0.34–0.53). At the end of Years 2, 3 and 4, monocytes were CT3.5=0.34×10⁹/L (0.28–0.45), 0.36×10⁹/L (0.28–0.48), and 0.36×10⁹/L (0.26–0.44), respectively. For PBO, monocytes were 0.41×10⁹/L (0.30–0.51), 0.40×10⁹/L (0.32–0.50) and 0.42×10⁹/L (0.32–0.55) respectively.

Conclusions: These data, plus previously-reported ALC data, support the concept that CT selectivity reduces adaptive immune cell counts, with relatively minor impact on the innate immune system.

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:

Per Soelberg-Sorensen has served on advisory boards for Biogen, Merck, Novartis, Teva, MedDay Pharmaceuticals, and GSK; on steering committees or independent data monitoring boards in trials sponsored by Merck, Teva, GSK, and Novartis; has received speaker honoraria from Biogen Idec,

Merck Serono, Teva, Sanofi-Aventis, Genzyme, and Novartis. His department has received research support from Biogen, Merck, Teva, Novartis, Roche, and Genzyme.

Fernando Dangond is an employee of EMD Serono, Inc., Billerica, USA, a business of Merck KGaA, Darmstadt, Germany.

Christine Hicking is an employee of Merck KGaA, Darmstadt, Germany.

Gavin Giovannoni has received speaker honoraria and consulting fees from Abbvie, 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.