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Durable suppression of MRI disease activity and slowing of brain volume loss in alemtuzumab-treated patients with active RRMS: 7-year follow-up of CARE-MS I (TOPAZ Study)

S. Schippling[1], D. Arnold[2], M. Barnett[3], G. Comi[4], C. Laganke[5], A. Rovira[6], A. Traboulsee[7], M. Melanson[8], N. Daizadeh[8], K. Nakamura[9], B. van Wijmeersch[10], D. Pelletier[11], O.B.O.T.C.-M.I.C. and Topaz Investigators[8]
[1]Neuroimmunology and Multiple Sclerosis Research, University Hospital Zurich and University of Zurich, Zurich, Switzerland, [2]NeuroRx Research, Montreal, Quebec, and Montreal Neurological Institute, McGill University, Montreal, Canada, [3]University of Sydney, Sydney, Australia, [4]University Vita-Salute San Raffaele, Milan, Italy, [5]North Central Neurology Associates, Cullman, USA, [6]Vall d'Hebron University Hospital, Barcelona, Spain, [7]The University of British Columbia, Vancouver, Canada, [8]Sanofi, Cambridge, USA, [9]Cleveland Clinic, Cleveland, USA, [10]Hasselt University, Hasselt, Belgium, [11]University of Southern California, Keck School of Medicine, Los Angeles, USA

Background and aims: In CARE-MS I (NCT00530348), alemtuzumab (12mg/day, baseline: 5 days; 12 months later: 3 days) demonstrated significant improvements in MRI outcomes, and reduced brain volume loss (BVL) versus SC IFNB-1a over 2 years (y). Alemtuzumab efficacy was durable in a 4-y extension (NCT00930553; 95% of CARE-MS I patients enrolled, 92% completed Y6), in which patients could receive alemtuzumab retreatment as needed for relapse/MRI activity or receive other DMTs per investigator's discretion. Further evaluation is ongoing (TOPAZ; NCT02255656). We present MRI lesion/BVL outcomes over 7 y (2 y core study plus 4 y extension, and TOPAZ Y1) in alemtuzumab-treated CARE-MS I patients.
Methods: Assessments: Annual MRI for disease activity (scored as new Gd-enhancing lesions; new/enlarging T2 lesions), new T1 hypointense lesions, and BVL (derived by relative change in brain parenchymal fraction [BPF]).
Results: 299 patients (93%) completed TOPAZ Y1. After the initial 2 courses, 59% received neither alemtuzumab nor another DMT. At Y7, patients were free of MRI disease activity (68%), new Gd-enhancing lesions (91%), new/enlarging T2 lesions (68%), and new T1 hypointense lesions (85%). Median BPF change from baseline was –0.59%, –0.87%, –0.98%, –1.13%, –1.37%, –1.43%, and –1.62% in Y1–7, respectively. Median annual BPF change was reduced versus SC IFNB-1a over 2 y, remaining low in Y3–7 (Y3: –0.19%, Y4: –0.14%, Y5: –0.20%, Y6: –0.17%, Y7: –0.16%).
Conclusion: Alemtuzumab durably reduced MRI disease activity and slowed BVL over 7 y in treatment-naive patients. Alemtuzumab provides a unique treatment approach for RRMS patients, offering durable efficacy without continuous treatment.

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Cladribine tablets produce selective and discontinuous reduction of B and T lymphocytes and natural killer cells in patients with early and relapsing Multiple Sclerosis

O. Stuve[1], P. Soelberg-Sorensen[2], G. Giovannoni[3], T. Leist[4], Y. Hyvert[5], D. Damian[5], U. Boschert[5]
[1]University of Texas, Southwestern Medical Center, Dallas, USA, [2]Department of Neurology, Danish MS Center, Copenhagen University Hospital, Copenhagen, Denmark, [3]Blizard Institute, Queen Mary University of London, London, United Kingdom, [4]Thomas Jefferson University, Philadelphia, USA, [5]EMD Serono, Inc,, Billerica, USA

Background and aims: Efficacy of cladribine tablets 3.5 mg/kg (CT3.5) has been demonstrated in patients with early MS (ORACLE-MS) and in patients with relapsing MS in the CLARITY and CLARITY-Extension studies. Here, we evaluate B and T lymphocyte and natural killer (NK) cell profiles after the first administration CT3.5 in ORACLE-MS, CLARITY and CLARITY-Extension.
Methods: Longitudinal evaluation of peripheral blood lymphocyte subtypes was conducted for patients receiving the first course of CT either as part of the initial 3.5 mg/kg active treatment groups (ORACLE-MS and CLARITY) or the placebo switched to active treatment groups (CLARITY-Extension). Absolute lymphocyte counts (ALC) and lymphocyte subtype dispositions were evaluated at baseline, and Weeks 5, 13, 24 and 48.
Results: Baseline distributions of ALC were similar across studies. Temporal profiles of CD19+ B lymphocytes and CD4+ and CD8+ T lymphocytes were consistent across studies. Rapid reductions were observed for CD19+ B-cells (~75% reduction at Week 5 in each study), with nadir at ~Week 13 (Figure 1). Reconstitution of CD19+ B-cells towards baseline value occurred from Week 24 to 48. Lesser, discontinuous reductions also occurred for CD4+ and CD8+ T-cells that had not fully returned to baseline by Week 48. CD16+/CD56+ NK cells were also transiently reduced with CT, with recovery evident at Weeks 24 and 48.
Conclusion: CT3.5 achieved an early and discontinuous reduction of peripheral blood B-cells, with rapid reconstitution to baseline, and a moderate, discontinuous reduction of T-cells. Treatment with CT is associated with early, transient NK cell reductions.

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