

Efficacy of a Third Course of Alemtuzumab in Patients With Active Relapsing-Remitting Multiple Sclerosis Who Experienced Disease Activity After the Initial Two Courses: Pooled Analysis of CARE-MS I and II

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SHORT TITLE: Efficacy of Alemtuzumab Retreatment

Background: Alemtuzumab improved clinical and MRI outcomes in 2-year (y), phase 3 trials vs SC IFNB-1a in RRMS patients (CARE-MS I: treatment-naive [NCT00530348]; CARE-MS II: inadequate response to prior therapy [NCT00548405]). Patients continuing in an extension study (NCT00930553) demonstrated durable efficacy through Y6, with 24% (CARE-MS I) and 30% (CARE-MS II) receiving a third course (C3).

Objective: Evaluate alemtuzumab retreatment efficacy in pooled CARE-MS I/II patients receiving a third course due to disease activity.

Methods: Patients received 2 alemtuzumab courses (baseline: 5 days; 12 months later: 3 days) in CARE-MS I and II. Patients entering the extension could receive as-needed alemtuzumab retreatment (for relapse and/or MRI activity) or another DMT (investigator discretion). Assessments: annualised relapse rate (ARR); mean EDSS change; improved/stable EDSS (vs core study baseline); 6-month confirmed disability improvement (CDI). Patients who received >3 courses or another DMT were excluded.

Results: Through Y6, 90% of pooled CARE-MS I/II patients entering the extension remained on study; 27% received a third course (of which Y2: 2%, Y3: 31%, Y4: 27%, Y5: 23%, Y6: 17%) without further

retreatment or other DMT. Mean time between C2 and C3 was 2.6 y. ARR decreased from 0.74 during the 12 months before C3 to 0.06 during the 12 months after ($P<0.0001$), and remained low (0.08) 3 y after C3. Mean EDSS change 12 months after C3 was -0.12 . Percentage of patients with stable/improved EDSS vs baseline increased from 62% at the time of C3 administration to 71% 12 months after C3; percentage with CDI increased from 5.0% to 17.5% ($P=0.0117$).

Conclusion: In CARE-MS patients receiving a third course due to disease activity, alemtuzumab effectively reduced relapses and improved disability without subsequent treatment. These data support administering a third alemtuzumab course in patients with disease activity following the second course to achieve durable outcomes.

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