

Low Conversion Rate From Relapsing-Remitting MS to Secondary Progressive MS in Patients Treated With Alemtuzumab: 6-Year Follow-up of CARE-MS I and II

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SHORT TITLE: Low Rates of SPMS Conversion With Alemtuzumab

Background: In the MSBase cohort (17,356 MS patients; median baseline disease duration: 3.8 years; median follow-up: 5.8 years), 18% of patients converted to SPMS using a definition based on EDSS scores and relapses (Lorscheider et al [*Brain* 2016;139:2395-405]). In alemtuzumab clinical trials of patients with active RRMS who were treatment-naïve (CARE-MS I; NCT00530348) or had an inadequate response (≥ 1 relapse) to prior therapy (CARE-MS II; NCT00548405), relapse rates were low and EDSS scores were stable/improved in the majority of patients over 6 years, without continuous treatment (NCT00930553).

Objective: To determine the SPMS conversion rate through 6 years among CARE-MS I and II alemtuzumab-treated patients.

Methods: In CARE-MS I and II, patients (N=811; median baseline disease duration: 2.8 years) received 2 alemtuzumab 12-mg courses (baseline: 5 consecutive days; 12 months later: 3 consecutive days); and in the extension, as-needed alemtuzumab for relapse or MRI activity or received another DMT per investigator's discretion. Lorscheider's optimal SPMS definition: disability progression in absence of relapse, worsening by 1 EDSS point in patients with EDSS ≤ 5.5 or 0.5 EDSS points in patients with EDSS ≥ 6 , confirmed over ≥ 3 months within the leading Functional System (FS), in patients with EDSS score ≥ 4 and pyramidal FS score ≥ 2 . Sensitivity analyses evaluated different confirmation periods and/or a minimum EDSS of 3.

Results: Compared with 18% in the MSBase cohort, only 1.1% and 3.7% of alemtuzumab-treated CARE-MS I and II patients, respectively, converted to SPMS through 6 years (2.5% pooled). Sensitivity analyses

confirmed the low conversion rates. 93% and 88% of alemtuzumab-treated patients who entered the extension remained on study through Year 6; 63% and 50% received no additional treatment (alemtuzumab or other DMT).

Conclusion: A low percentage (2.5%) of CARE-MS alemtuzumab-treated patients progressed to SPMS according to criteria developed by Lorscheider. Further confirmation in real-world cohorts is needed.

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