Objective: Compare lymphocyte pharmacodynamics over 2 years in alemtuzumab-treated relapsing-remitting MS (RRMS) patients with improved, worsened, or stable disability through 6 years.

Background: In the phase 3 CARE-MS studies (NCT00530348; NCT00548405), alemtuzumab 12 mg/day (baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes versus subcutaneous IFNB-1a over 2 years in patients with active RRMS. Efficacy was maintained in a 4-year extension (NCT00930553) without continuous treatment; 53% of patients received no additional alemtuzumab or other disease-modifying therapy. The effects of alemtuzumab over time may be due to its selective depletion and distinctive repopulation of circulating CD52-expressing T and B lymphocytes.

Design/Methods: Blood counts were obtained monthly; lymphocytes were phenotyped by flow cytometry quarterly and at Months 1 and 13 (1 month after alemtuzumab Courses 1 and 2, respectively). Pharmacodynamic assessments (using pooled CARE-MS data [n=802]) included: total counts of lymphocytes, CD3+/CD4+/CD8+ T cells, and CD19+ B cells; CD4+/CD8+ naive/memory/regulatory (T_{reg}); and CD19+ immature/mature/memory. Ratios of CD19+ B cells (total/immature/memory) to CD4+ and CD8+ T_{reg} cell counts were also assessed. Relationship between lymphocyte repopulation patterns and disability was assessed in patients with 6-month confirmed disability worsening (CDW; ≥1.0-point Expanded Disability Status Scale [EDSS] increase [≥1.5 points if baseline EDSS=0]), 6-month confirmed disability improvement (CDI; ≥1.0-point EDSS decrease from baseline [assessed in patients with baseline EDSS ≥2.0]), or stable EDSS (neither CDW nor CDI).

Results: No significant overall difference in lymphocyte depletion or repopulation patterns was observed over 2 years in patients who experienced CDI, CDW, or neither through 6 years. No correlation was observed between CDI, CDW, or stable EDSS and any CD19+/T_{reg} ratio.

Conclusions: Differences in depletion and repopulation kinetics of the tested lymphocyte populations in the first 2 years after initiating alemtuzumab did not appear to be associated with improved, worsening, or stable disability in RRMS patients.