**OBJECTIVES**
- To evaluate brain volume loss (BVL) over 5 years in patients who received alemtuzumab in Core Study phase 3 trials and continued on an ongoing extension study.
- To evaluate the possible impact of baseline brain parenchymal fraction (BPF) on 5-year BVL.

**CONCLUSIONS**
- **Alemtuzumab slowed BVL through Year 5 in patients with active RRMS who had an inadequate response to prior therapy at baseline.**
  - For the overall alemtuzumab-treated population, median annual BVL was 0.022% in Years 2, 3, 4, and 5.
  - Baseline BPF did not impact BVL through Year 5.

- **Most patients did not receive alemtuzumab retreatment after the initial 2 courses in the core study through Year 5.**
  - Based on these findings, alemtuzumab provides a unique treatment approach with durable efficacy through 5 years in the absence of continuous treatment for RRMS patients.

**INTRODUCTION**
- **Alemtuzumab** is a humanized anti-CD52 monoclonal antibody that is approved for the treatment of relapsing-remitting multiple sclerosis (RRMS) in >50 countries.
- In patients with active RRMS who had an inadequate response (≥1 relapse after 5 months of treatment) to prior therapy, alemtuzumab (CARE-MS II) demonstrated greater improvements in clinical and MRI outcomes versus SC IFNB-1a over 2 years, and alemtuzumab patients were more likely to have no evidence of disease activity versus SC IFNB-1a patients.
- The most frequent adverse events (AEs) observed with alemtuzumab were infusion-related reactions; other AEs of interest included autoimmune AEs.
- Alemtuzumab-treated patients who have been followed through 5 years in the ongoing open-label extension study (NCT00305937) continue to show durable efficacy outcomes despite most receiving no alemtuzumab since Month 12 and no other disease-modifying therapy (DMT).
- Brain atrophy is a marker for neurodegeneration in RRMS patients and has been correlated with disability worsening and cognitive impairment.
- Recent literature shows that irreversible BVL, in excess of that observed in healthy individuals in patients with active RRMS who had an inadequate response (≥1 relapse after 5 months of treatment) to prior therapy, occurs early in the MS disease course.

**METHODS**

**Study Design**
- **Core Study** was a phase 3, randomized, head-to-head, rater-blinded, 2-year study of alemtuzumab versus SC IFNB-1a (44 µg 3 times per week) in patients with active RRMS who had an inadequate efficacy response to prior therapy (≥1 relapse at baseline).
- Patients randomized to alemtuzumab received 2 courses of 12 mg (given in 3 consecutive days at baseline and on 3 consecutive days 12 months later).
- In the ongoing extension study, patients could receive alemtuzumab retreatment (12 mg on 3 consecutive days 1 year after the most recent course) for relapse or MRI activity.
- Retreatment criteria were 1 protocol-defined relapse, or ≥2 new T2 lesions, hypointense and/or new gadolinium-enhancing T2 brain, or spinal cord lesions on MRI.
- Use of other DMTs was permitted at the investigator’s discretion.

**RESULTS**

**Efficacy Assessments**
- MRI scores were obtained at baseline and annually thereafter, and analyzed centrally at NeuroRx (Montreal, Canada) by experts masked to treatment group assignment.
- BVL was derived by BPF change, and scans were read by Cleveland Clinic (Cleveland, OH, USA).
- BVL was compared in patient subgroups stratified by baseline median BPF value.
- Retreatment analyses were performed on patients with available BPF value at baseline.

**Statistical Analyses**
- Percentage changes in BPF were analyzed using the Wilcoxon signed rank test.
- Interim analyses were based on all available data through Year 3 of the ongoing extension study (Figure 3).

**RESULTS**

- **Brain Volume Change by Year**
  - Alemtuzumab was slowed BVL by 24% over 24 months versus SC IFNB-1a at the end of the core study phase 2 (Figure 3).
  - The slowing of BVL in alemtuzumab patients was maintained through 5 years.

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**Figure 2. Alemtuzumab Retreatment Rate in CARE-MS II Was Low Through 5 Years**

- A total of 435 patients received alemtuzumab 12 mg in CARE-MS II; of the 423 alemtuzumab patients with complete data, 365 (86%) patients entered the extension study.
- Through 5 years, 218 (55%) patients did not receive retreatment with alemtuzumab or other DMT.
- Over 5 years, there were 209 retreatments in 158 patients.
- The figure shows that retreatment criteria were met for 154 retreatments (78% of all retreatments).
- Interim analyses were based on all available data through Year 3 of the ongoing extension study (Figure 3).

**Figure 3. Slowing BVL Through 5 Years in Alemtuzumab-Treated Patients**

- Median yearly BVL was decreased at Year 2 in CARE-MS II alemtuzumab-treated patients and this decrease was maintained through Year 5 (Figure 4).

**Figure 4. Slowing BVL Through 5 Years in Alemtuzumab-Treated Patients**

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**Figure 5. Baseline BPF Did Not Impact BPF Change From Baseline Through 5 Years in Alemtuzumab-Treated Patients**

- Baseline BPF did not impact BPF change from baseline through 5 years in allemtuzumab-treated patients (Figure 5).

**Figure 6. Baseline BPF Did Not Impact Median Yearly BPF Change Through 5 Years in Alemtuzumab-Treated Patients**

- Baseline BPF did not impact median yearly BPF change through 5 years in allemtuzumab-treated patients (Figure 6).

**References**


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