DX17

Patients With Highly Active RRMS Despite Prior Therapy Show Durable Improvement With Alemtuzumab Over 5 Years

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OBJECTIVE

- **To evaluate 5-year efficacy in a subset of patients with RRMS and highly active disease at baseline who were treated with alemtuzumab in CARE-MS II**

CONCLUSIONS

- **Efficacy of alemtuzumab in patients with highly active RRMS despite an inadequate response to prior therapy was durable in the extension through Year 5 despite most not receiving treatment since Month 12 (4 years of no retreatment)**
- **Based on these findings, alemtuzumab may provide a unique treatment approach with durable efficacy in the absence of continuous treatment for patients with highly active RRMS**

INTRODUCTION

- Alemtuzumab is a humanized anti-CD52 monoclonal antibody that is approved for the treatment of RRMS in >50 countries
- In the CARE-MS II study (NCT00548405), alemtuzumab demonstrated greater improvements in clinical and MRI outcomes over 2 years than SC IFNB-1a in patients with active RRMS and an inadequate response (≥1 relapse) to a prior therapy at baseline[1]
- In an ongoing extension study (NCT00930553), alemtuzumab showed durable efficacy on clinical and MRI outcomes through Year 5, during which most patients did not receive alemtuzumab after the initial 2 courses in the core study, or another disease-modifying therapy (DMT)[2,3]
- The most frequent adverse events (AEs) observed with alemtuzumab were infusion-associated reactions; other AEs of interest included autoimmune AEs[1]
- A number of prognostic factors predict risk for disability worsening (increasing Expanded Disability Status Scale [EDSS] score) in patients with MS, including MRI burden, interval between relapses, relapse frequency, and degree of relapse recovery[4]
- Patients with highly active RRMS may be considered a group with prognostic features predictive of disability worsening

METHODS

Study Design

- CARE-MS II was a phase 3, randomized, head-to-head, rater-blinded, 2-year study versus SC IFNB-1a (44 µg 3 times per week)[1]
  - Patients who were randomized to alemtuzumab 12 mg/day received 2 annual courses (on 5 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)[2]
  - Alemtuzumab retreatment criteria were ≥1 protocol-defined relapse, or ≥2 new/enlarging T_2 hyperintense and/or new gadolinium (Gd)-enhancing T_1 brain or spinal cord lesions on MRI
- Use of other DMTs was permitted at the investigator's discretion

Highly Active Disease Definition

- ≥2 relapses in the year prior to randomization and ≥1 Gd-enhancing lesion at core study baseline

Assessments

- Annualized relapse rate (ARR) and proportion of patients free of relapse[a]
- EDSS score was assessed quarterly by blinded raters
- Six-month confirmed disability worsening (CDW): increase from core study baseline of ≥1.0 EDSS point (or ≥1.5 points if baseline EDSS score=0)
- Confirmed disability improvement (CDI): decrease from core study baseline by ≥1.0 EDSS point confirmed over 6 months, in patients with baseline EDSS score ≥2.0
- Proportion of patients with improved (≥1-point decrease) or stable (≤0.5-point change) EDSS scores versus baseline
- MRI was conducted annually
- No evidence of disease activity (NEDA) was defined as the absence of clinical disease activity (relapses and 6-month CDW) and MRI disease activity (new Gd-enhancing T_1 lesions and new/enlarging T_2 hyperintense lesions)

Statistical Analyses

- Interim analyses were based on all available data through Year 3 of the ongoing extension study (up to the data cut-off date of 4 October 2014; 5-year total follow-up) in patients with highly active disease at baseline who had received alemtuzumab in the core CARE-MS II study
- Kaplan-Meier estimates were used for assessing the proportion of patients with no evidence of 6-month CDW or those who achieved 6-month CDI through 5 years
- Proportions of patients with no evidence of clinical or MRI disease activity were analyzed descriptively with percentages, and CIs were obtained using the normal approximation to the binomial distribution

RESULTS

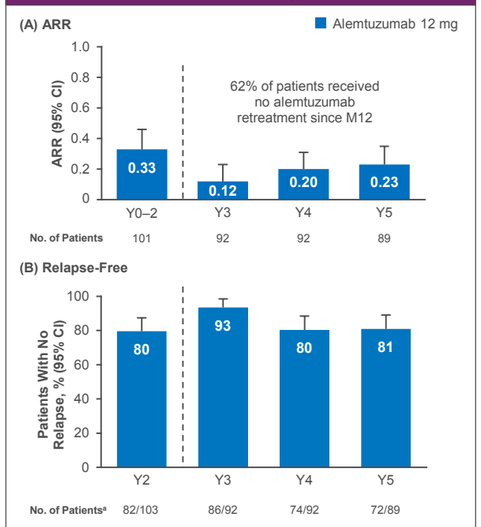
Patients

- Of 435 patients treated with alemtuzumab 12 mg in CARE-MS II, 103 patients (24%) met highly active disease criteria at core study baseline
- 92 (89%) of the 103 highly active patients entered the extension study; of these, 89 (97%) remained on study through Month 60 (Year 5)
- Through 5 years, 57 patients (62%) received no alemtuzumab retreatment since the initial 2 courses at core study baseline and Month 12 and no other DMT
  - 57 (62%) patients did not receive retreatment with alemtuzumab
  - 89 (97%) patients did not receive another DMT

Efficacy

- ARR remained low in each individual year of the extension study (**Figure 1A**)
  - Over Years 0–5, ARR was 0.23 (95% CI, 0.17–0.30)
  - At least 80% of patients were free of relapse in each year (**Figure 1B**)
- Over Years 0–5, most patients had no evidence of 6-month CDW and 45% achieved CDI (**Table 1**)
  - Of those who achieved 6-month CDI, 94% had no evidence of 6-month CDW
- Most patients showed improved or stable EDSS scores through Years 0–5 (**Figure 2**)

Figure 1. Durable Efficacy of Alemtuzumab on Relapses in Each Year of the Extension Study

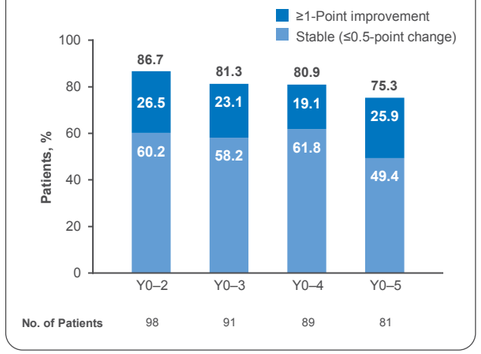


[a]Denominator is number of patients evaluated for relapse-free outcome
M=month; Y=year

Table 1. Disability Outcomes in the Highly Active Subgroup

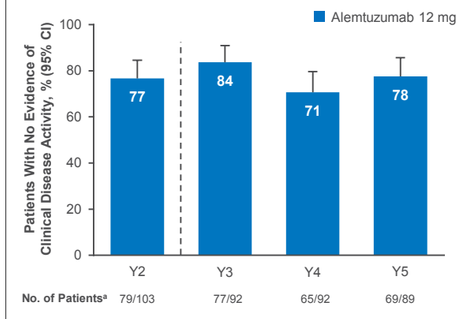
Outcome	Highly Active Patients Y0–5
Mean EDSS score change from baseline to Year 5	+0.03
Patients with no evidence of 6-month CDW, %	74.5
Patients achieving 6-month CDI, %	44.9

Figure 2. Durable Efficacy on Disability Through 5 Years



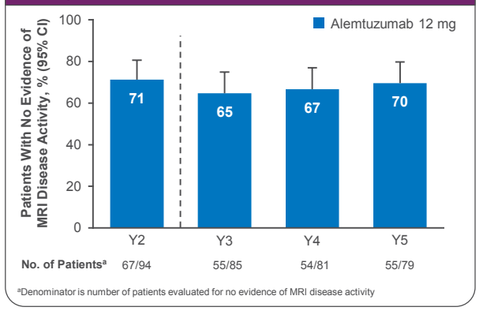
- Most patients had no evidence of clinical and MRI disease activity in each year of the extension study (**Figures 3 and 4**)

Figure 3. Most Patients Had No Evidence of Clinical Disease Activity in Each Year of the Extension Study



[a]Denominator is number of patients evaluated for no evidence of clinical disease activity

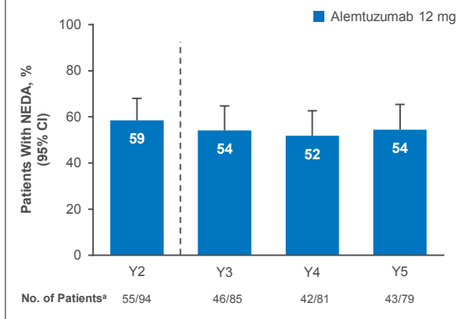
Figure 4. Most Patients Had No Evidence of MRI Disease Activity in Each Year of the Extension Study



[a]Denominator is number of patients evaluated for no evidence of MRI disease activity

- More than half of patients achieved NEDA in each year of the extension study (**Figure 5**)
  - 26% of patients had NEDA sustained over Years 3–5 (Months 24–60)

Figure 5. Durable Efficacy of Alemtuzumab on NEDA in Each Year of the Extension Study



[a]Denominator is number of patients evaluated for NEDA

References

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CARE-MS=Comparison of Alemtuzumab and Rebif® Efficacy in Multiple Sclerosis
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Alemtuzumab is approved in many countries around the world for treatment of adults with relapsing forms of MS. In the US, the indication provides that, because of its safety profile, the use of alemtuzumab should be reserved for patients who generally have had an inadequate response to 2 or more therapies indicated for the treatment of MS. In the EU, it is approved to treat patients with relapsing-remitting MS with active disease defined by clinical or imaging features. This material may contain information that is outside of the approved labeling in some countries.

[a]Relapses were confirmed per the protocol definition by an independent, blinded relapse adjudication panel in the core study; in the extension study, relapses were confirmed per the protocol definition by the investigator.

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