DX29

No Evidence of Disease Activity for 4 Years Following 2 Courses of Alemtuzumab and No Further Treatment: Long-term Responders From CARE-MS II

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OBJECTIVE

- **To evaluate patients who had no evidence of disease activity (NEDA) beginning in Year 2 of the core CARE-MS II study and had no further treatment following the initial 2 courses**

CONCLUSIONS

- **Among alemtuzumab-treated CARE-MS II patients who achieved NEDA in Year 2 and received no further treatment following the 2 initial courses of alemtuzumab at Month 0 and Month 12, most had NEDA in each year of the extension study and nearly half attained sustained NEDA through Year 5**
- **Based on these findings, alemtuzumab may provide a unique treatment approach with durable efficacy in the absence of continuous treatment for RRMS patients**

INTRODUCTION

- Alemtuzumab is a humanized anti-CD52 monoclonal antibody approved for the treatment of RRMS in >50 countries
- Patients with active RRMS who were either treatment-naive (CARE-MS I, NCT00530348)[1] or who had an inadequate response (≥1 relapse) to prior therapy at baseline (CARE-MS II, NCT00548405)[2], demonstrated greater improvements on clinical and MRI outcomes, and were more likely to achieve NEDA, with alemtuzumab than with SC IFNB-1a
- The most frequent adverse events (AEs) with alemtuzumab were infusion-associated reactions (IARs); other AEs of interest included autoimmune AEs[1,2]
- Alemtuzumab showed durable efficacy on clinical and MRI outcomes through 5 years in an ongoing extension study (NCT00930553), even though most patients did not receive alemtuzumab retreatment since Month 12 or another disease-modifying therapy (DMT)[3,4]

METHODS

Study Design

- CARE-MS II was a randomized, rater-blinded, active-controlled, head-to-head, phase 3 trial of alemtuzumab versus SC IFNB-1a (44 µg 3 times per week) in patients with active RRMS who had an inadequate response (≥1 relapse) to prior therapy at baseline[2]
  - Patients randomized to alemtuzumab 12 mg/day IV 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)[5]
  - 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

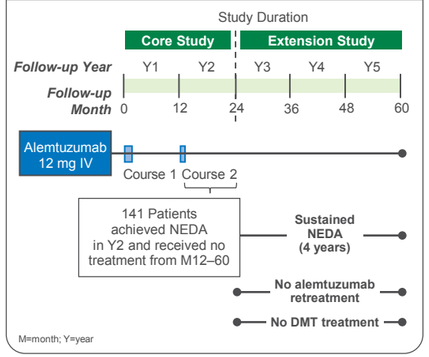
Efficacy Assessments

- Six-month confirmed disability worsening was assessed by blinded raters and defined as an increase of ≥1.0 Expanded Disability Status Scale (EDSS) point (or ≥1.5 points if baseline EDSS=0)
- NEDA was defined as no evidence of clinical disease activity (relapse[a] and 6-month confirmed disability worsening) and MRI disease activity (new Gd-enhancing T_1 and new/enlarging T_2 hyperintense lesions)
- MRI scans were obtained at baseline and annually thereafter, and analyzed centrally at NeuroRx Research (Montréal, Canada) by experts masked to treatment group assignment
- Brain volume loss (BVL) was derived from brain parenchymal fraction (BPF) change, and scans were read at Cleveland Clinic (Cleveland, OH, USA)

Statistical Analysis

- This analysis included patients who achieved NEDA in Year 2 and received no alemtuzumab retreatment since Month 12 or other DMT (**Figure 1**)
  - BPF analyses included patients who had NEDA sustained from Year 2 through Year 5 and received no additional treatment
- Interim analyses were based on all available data through Year 3 of the ongoing extension study (5-year total follow-up)
- Proportions of patients with clinical and MRI disease activity were analyzed descriptively with percentages
- Median percentage change in BPF from baseline and annual change in BPF are reported, with 95% CIs

Figure 1. CARE-MS II Core and Extension Study Design and Methodology for Describing Patients With 4-Year Sustained NEDA



RESULTS

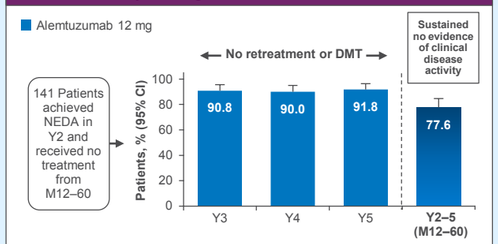
Patients

- Of the alemtuzumab-treated patients who completed CARE-MS II, 393 (93%) enrolled in the extension study
  - 141 patients achieved NEDA in core study Year 2 and received no additional treatment in the extension study (ie, no treatment for 4 years following the second course at Month 12 in the core study)

Patients Who Achieved NEDA in Year 2 and Had No Additional Treatment Since Month 12

- In this cohort, most patients had no evidence of clinical disease activity in individual Years 3, 4, and 5 of the extension study, and 78% had no evidence of clinical disease activity sustained over Years 2–5 (**Figure 2**)
- Most patients had no evidence of MRI disease activity in individual Years 3, 4, and 5 of the extension study, and 59% had no evidence of MRI disease activity sustained over Years 2–5 (**Figure 3**)
- Most patients had NEDA in individual Years 3, 4, and 5 of the extension study (**Figure 4**)
- 52 patients (48%) had NEDA sustained over Years 2–5 without receiving any alemtuzumab retreatment or other DMT in the extension study

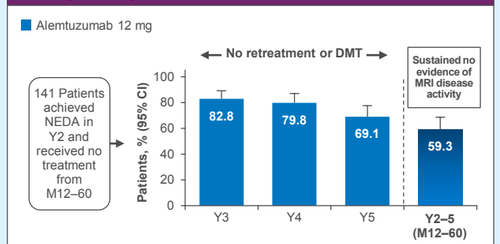
Figure 2. Most Patients Had No Evidence of Clinical Disease Activity Through Year 5



	Y3	Y4	Y5	Y2–5 (M12–60)
No. of Patients[a]	128/141	126/140	123/134	104/134
No evidence of relapse	95.0%	94.3%	94.0%	84.3%
No evidence of 6-month confirmed disability worsening	95.7%	93.6%	97.8%	91.0%

[a]Denominator is number of patients evaluated for clinical disease activity

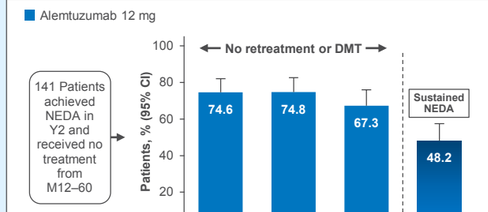
Figure 3. Most Patients Had No Evidence of MRI Disease Activity Through Year 5



	Y3	Y4	Y5	Y2–5 (M12–60)
No. of Patients[a]	111/134	95/119	76/110	64/108
Gd-enhancing T_1 lesion-free	94.0%	96.7%	92.5%	89.0%
New/enlarging T_2 hyperintense lesion-free	83.6%	80.8%	69.1%	59.3%

[a]Denominator is number of patients evaluated for MRI disease activity

Figure 4. Almost Half of Patients Had NEDA Sustained Through Year 5



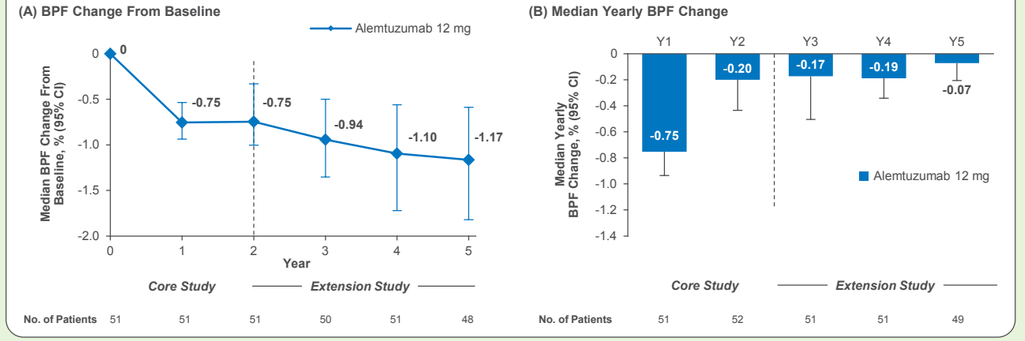
	Y3	Y4	Y5	Y2–5 (M12–60)
No. of Patients[a]	100/134	89/119	74/110	52/108

[a]Denominator is number of patients evaluated for NEDA

Slowing of BVL in Patients With Sustained NEDA in Years 2–5 and No Additional Treatment Since Month 12

- Median rate of yearly BVL remained low through the extension (**Figure 5**)

Figure 5. Slowing BVL Through 5 Years in Patients With Sustained NEDA and No Retreatment



No. of Patients						
(A) BPF Change From Baseline	51	51	51	50	51	48
(B) Median Yearly BPF Change	51	52	51	51	49	

References

1. Cohen JA, Coles AJ, Arnold DL, et al. *Lancet* 2012;380:1819-28. 2. Coles AJ, Twyman CL, Arnold DL, et al. *Lancet* 2012;380:1829-39. 3. Havrdova E, Arnold DL, Cohen JA, et al. *Mult Scler* 2015;21(suppl 11):Platform 152. 4. Fox E, Arnold DL, Cohen JA, et al. *Mult Scler* 2015;21(suppl 11):P1102. 5. Fox EJ, Arnold DL, Cohen JA, et al. *Neurology* 2013;80:S41.001.

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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 multiple sclerosis (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 studies; in the extension study, relapses were confirmed per the protocol definition by the investigator.

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