CMSC 2015
Presentation DX05

Durable Effect of Alemtuzumab on MRI Activity and Brain Atrophy in Relapsing-Remitting Multiple Sclerosis Patients: 4-Year Follow-up of CARE-MS II

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on behalf of CARE-MS II Investigators

Presented by Anthony Traboulsee

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Disclosures

- **AT:** Consulting fees (Biogen, Chugai, Genzyme, MedImmune, Novartis, Roche, Serono, and Teva Innovation); principal investigator on clinical trials (Genzyme, Roche)
- **HPH:** Honoraria for consulting and speaking at symposia (Bayer Healthcare, Biogen Idec, CSL Behring, Genzyme, Merck Serono, Novartis, Octapharma, Roche, Teva, and Sanofi, with approval by the Rector of Heinrich Heine-University)
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- **LK:** Provides statistical support as a consultant to Genzyme
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CARE-MS=Comparison of Alemtuzumab and Rebif® Efficacy in Multiple Sclerosis.

CARE-MS II Study Background

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- Randomized, 2-year, rater-blinded, active-controlled, phase 3 trial in patients with an inadequate response, defined as at least one relapse, to a prior therapy[a]
- Alemtuzumab versus SC IFNB-1a:
  - 49% decrease in annualized relapse rate
  - 42% decrease in 6-month sustained accumulation of disability[1]
  - MRI outcomes were significantly improved:
    - More patients free from MRI activity[b]
    - Reduction in brain volume loss
- Consistent and manageable safety profile

U.S. indication: For the treatment of patients with relapsing forms of MS. 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 drugs indicated for the treatment of MS.
EU indication: Approved for patients with relapsing-remitting MS (RRMS) with active disease defined by clinical or imaging features.
[a]NCT00548405.
[b]Absence of both new gadolinium (Gd)-enhancing lesions and new/enlarging T_2 hyperintense lesions.
MRI=magnetic resonance imaging; SC IFNB-1a=subcutaneous interferon beta-1a
1. Coles AJ et al. *Lancet* 2012;380:1829-39.

Objective: To Examine the Effect of Alemtuzumab on MRI Outcomes Over 4 Years

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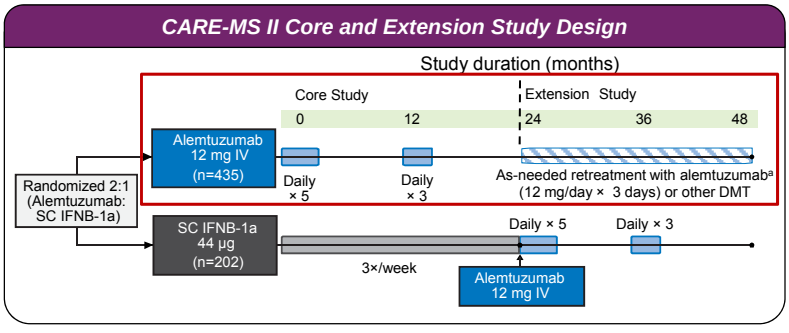

- Ongoing, open-label extension study[b] provides follow-up, retreatment when necessary, and re-assessment of outcomes through ≥ Month 60
  - 93% of alemtuzumab patients completing CARE-MS II enrolled in the extension study
  - Baseline characteristics of patients were similar to that of patients in the core study
  - Clinical efficacy of alemtuzumab was maintained over 4 years despite most patients not receiving alemtuzumab (68%) or other DMT over the previous 3 years[1]
  - Durable effects on MRI outcomes were observed at Year 3[2]

[a]Patients qualified for retreatment based on either one clinical episode or MRI evidence for new disease activity.
[b]NCT00930553.
DMT=disease-modifying therapy; IV=intravenous
1. Hartung HP et al. ACTRIMS-ECTRIMS 2014, P043; 2. Fisher E et al. ACTRIMS-ECTRIMS 2014, P103.

Extension Study – MRI and Safety Assessments

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MRI Assessments

- Study baseline and annually thereafter
- Standardized acquisition
- Read centrally by experts blinded to treatment status (NeuroRx)
- Brain volume loss (atrophy) measured by BPF change
  - Blinded scans read by Cleveland Clinic

Safety Assessments

- Adverse events and concomitant medications
- Laboratory assessments
- Monitoring to assess safety at baseline and monthly for 48 months after last infusion including complete blood counts with differential, serum creatinine, urinalysis with urine cell counts, and quarterly thyroid function test

Statistical Analyses

- Analyses were based on all available data through Year 2 of the extension (4-year total follow-up from the first alemtuzumab dose)

BPF=brain parenchymal fraction

Alemtuzumab Retreatment Rate Was Low Through 4 Years

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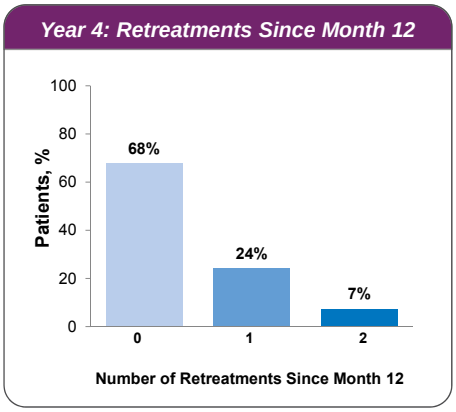

- 93% of alemtuzumab patients from CARE-MS II entered the extension
- 68% of patients did not receive retreatment with alemtuzumab over the 3 years since the initial 2 courses at Month 0 and 12 months later
- 95% did not receive other DMT in Years 3 and 4

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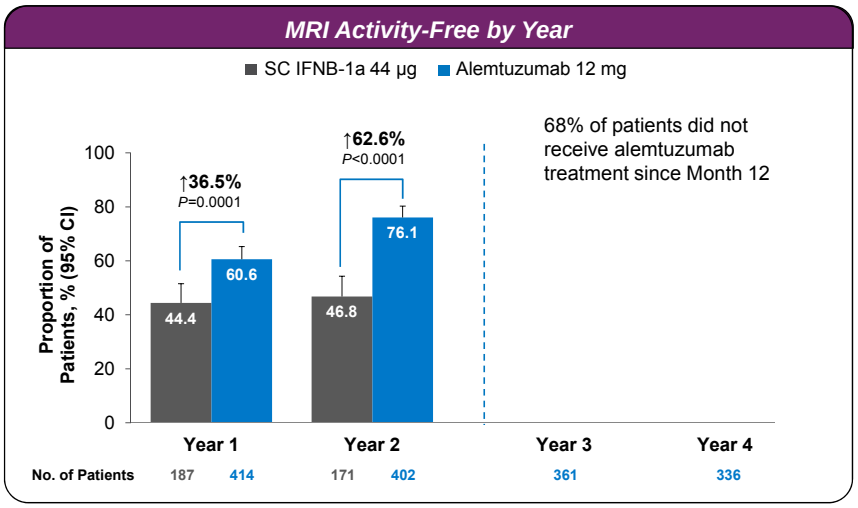
Durable Suppression of MRI Activity Through Year 4



- A majority of alemtuzumab patients were free of MRI activity in Years 3 and 4 despite most patients not receiving retreatment in the extension study

MRI activity-free: No new Gd-enhancing and new/enlarging T_2 hyperintense lesions.

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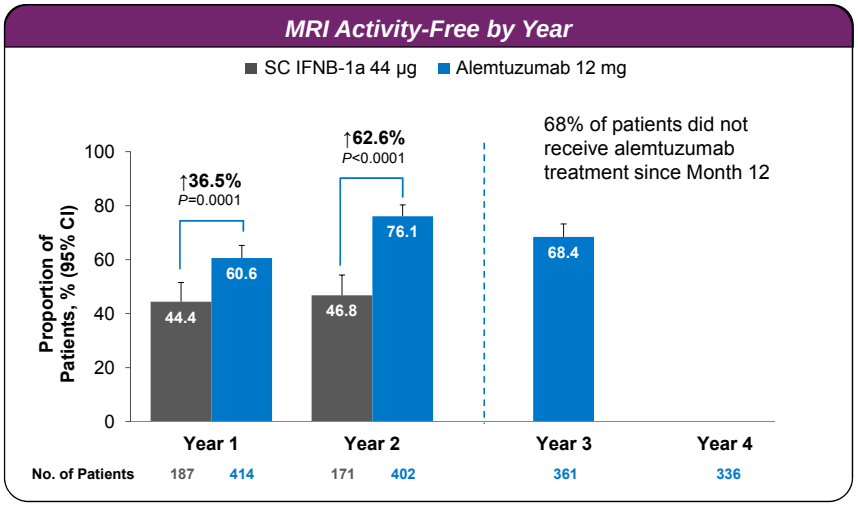
Durable Suppression of MRI Activity Through Year 4



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Durable Suppression of MRI Activity Through Year 4

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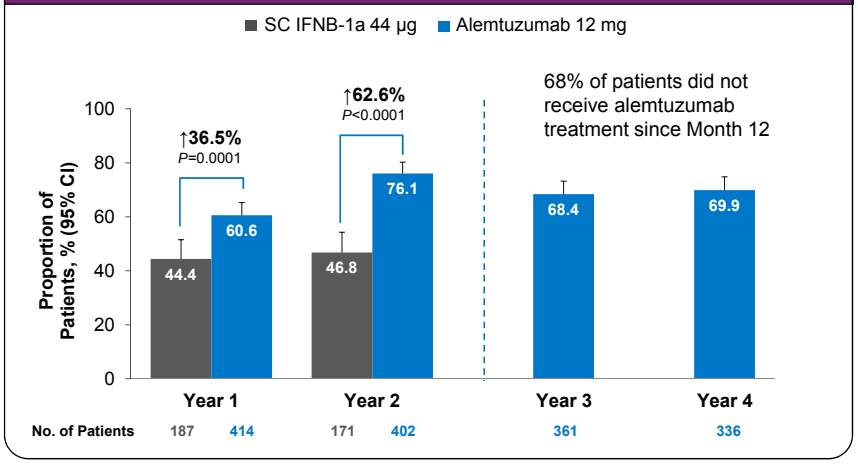
MRI Activity-Free by Year



- A majority of alemtuzumab patients were free of MRI activity in Years 3 and 4 despite most patients not receiving retreatment in the extension study

MRI activity-free: No new Gd-enhancing and new/enlarging T_2 hyperintense lesions.

Durable Suppression of New MRI Lesion Activity Through Year 4

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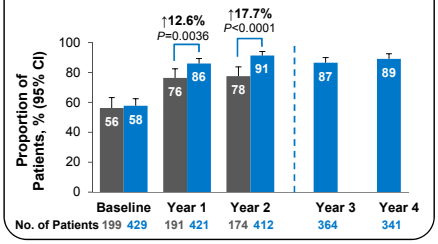
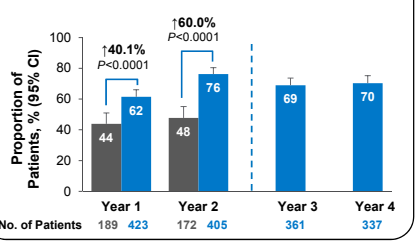
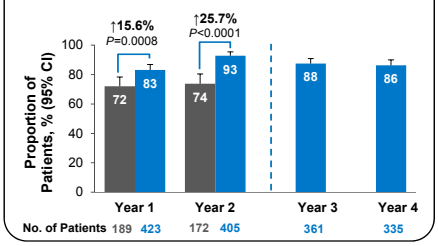
Gd-Enhancing T_1 Lesion-Free



New/Enlarging T_2 Lesion-Free



New Non-Enhancing T_1 Lesion-Free



SC IFNB-1a 44 µg
Alemtuzumab 12 mg

- 68% of patients did not receive alemtuzumab treatment since Month 12
- In Years 3 and 4, the proportions of patients Gd-enhancing T_1 lesion-free, new/enlarging T_2 lesion-free, or new non-enhancing T_1 lesion-free remained stable compared with the core study

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Distribution of New Gd-Enhancing Lesions in Alemtuzumab Patients Remained Stable Through Year 4

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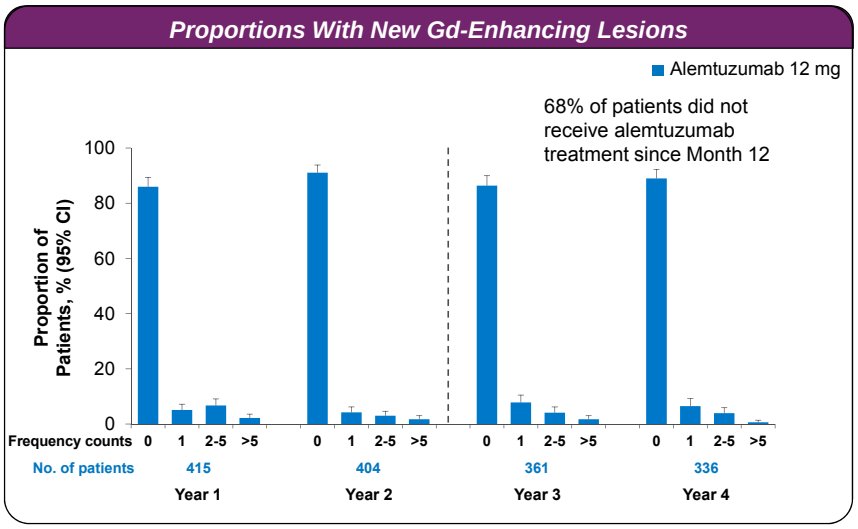

Distribution of New/Enlarging T_2 Lesions in Alemtuzumab Patients Remained Stable Through Year 4

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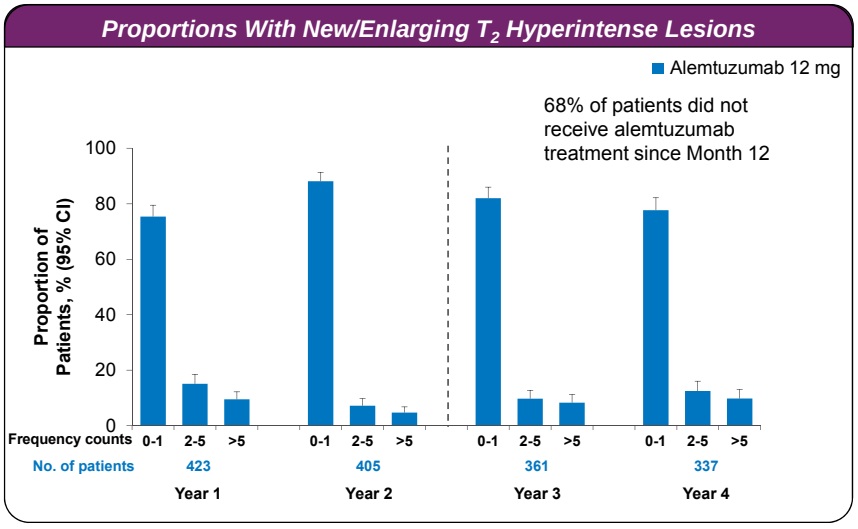

Count frequency ranges for new/enlarging T_2 hyperintense lesions reflect the retreatment eligibility criteria.

Distribution of New T_1 Lesions in Alemtuzumab Patients Remained Stable Through Year 4

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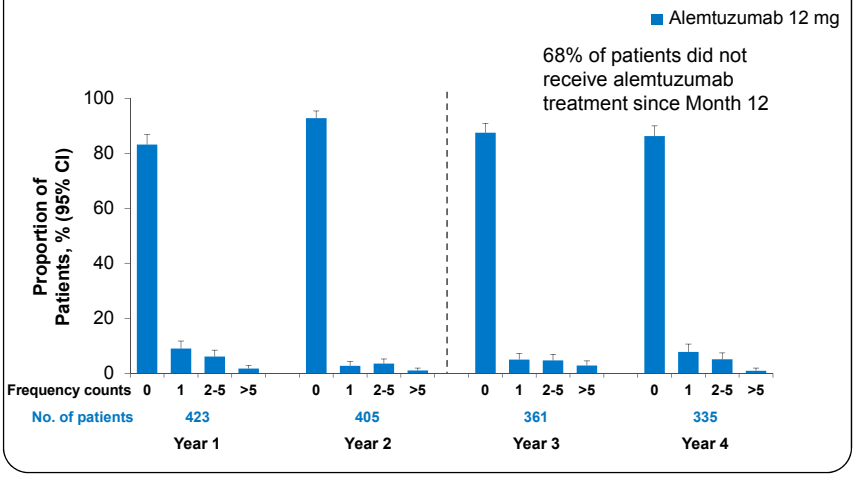
Proportions With New Non-Enhancing T_1 Hypointense Lesions



Durable Effect on No Evidence of Disease Activity Maintained Through Year 4

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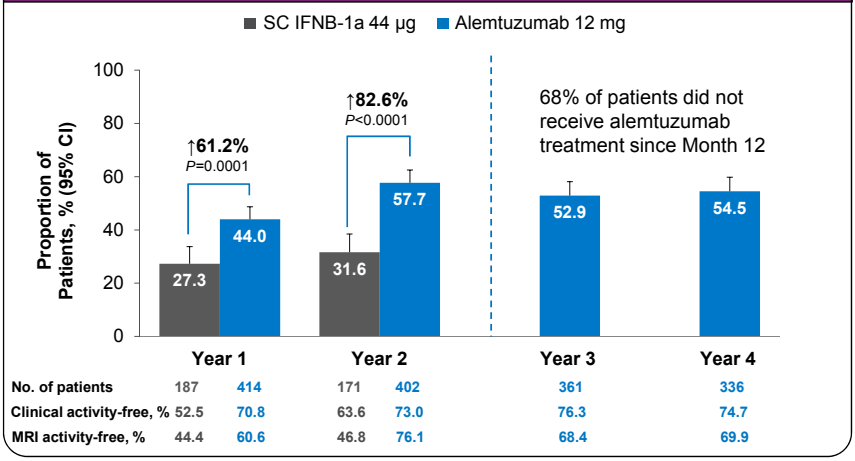
No Evidence of Disease Activity by Year



- The proportion of alemtuzumab patients achieving no evidence of disease activity was largely stable in Years 3 and 4

No evidence of disease activity: Absence of clinical disease activity (relapse and 6-month sustained accumulation of disability) and MRI activity (new Gd-enhancing lesions, and new/enlarging T_2 hyperintense lesions).

Slowing BPF Loss Over 4 Years in Alemtuzumab Patients

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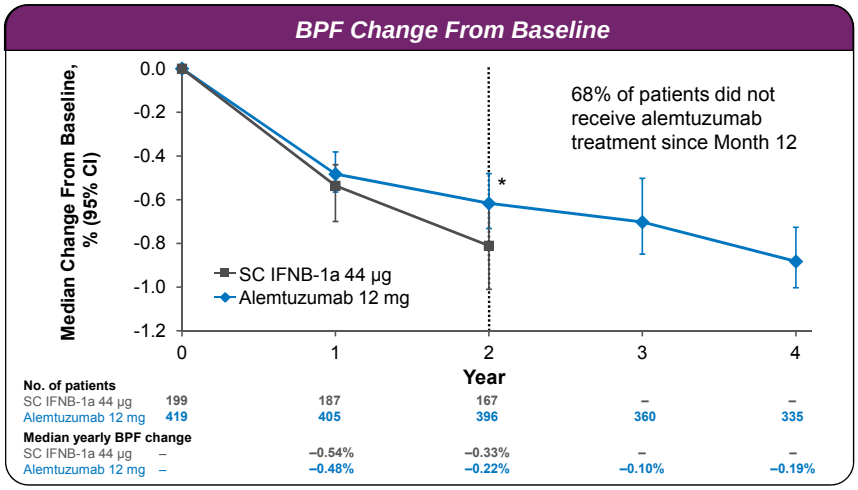

- Alemtuzumab slowed the reduction in BPF by 24% versus SC IFNB-1a at the end of the core CARE-MS II study
- Median yearly BPF loss was smaller in Years 3 and 4 than during the core study

*Alemtuzumab vs SC IFNB-1a, *P*=0.0121.

Conclusions: A durable treatment approach for RRMS

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- Majority of alemtuzumab patients remained free of new MRI activity in Year 4, with most patients receiving their last alemtuzumab treatment course 3 years prior
- The rate of brain atrophy remained low in Year 4
  - Median yearly brain volume loss was less than 0.2% in Years 3 and 4
- These results reflect a reduction in focal inflammation with alemtuzumab treatment
- The durable effects may be due to the distinct pattern of lymphocyte depletion and repopulation following treatment
- Together, these findings indicate that alemtuzumab represents a novel and durable treatment approach for RRMS

CARE-MS Study Group and Acknowledgments

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