Patients With Active RRMS and Inadequate Response to Therapy at Baseline Show Durable Disability Improvement Over 5 Years With Alemtuzumab: CARE-MS II

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Presented by Christopher LaGanke

CARE-MS II Study Background

- Phase 3 trial in patients with active RRMS and an inadequate response to prior therapy at baseline, defined as at least one relapse
- Alemtuzumab versus SC IFNB-1a over 2 years:
  - Significant 49% decrease in annualized relapse rate1
  - Significant 42% reduction in risk of 6-month confirmed disability worsening1
  - 68% more patients with no evidence of MRI disease activity2
  - Significant 24% reduction in brain volume loss1
- Most frequent adverse events (AEs) were infusion-associated reactions; other AEs of interest included autoimmune AEs1

CARE-MS II Study Background

- Ongoing, open-label, rater-blinded extension study provides follow-up, retreatment where necessary, and reassessment of outcomes through Month 60 (Year 5)
- 393 (93%) of alemtuzumab patients completing CARE-MS II (Years 1 and 2) enrolled in the extension (Year 3–5)
- 357 (91%) remained on study through Month 60 (end of Year 5)

Disclosures

- Christopher LaGanke: Compensation for consulting (Acorda Therapeutics, Bayer, Biogen, Cephalon, EMD Serono, Novartis, Pfizer, Questcor, Sanofi Genzyme, Strativia, Teva, and UCB).
- Aaron Boster: Consulting fees and/or fees for non-CME services (Biogen, Mallinckrodt, Medtronic, Novartis, Sanofi Genzyme, and Teva).
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CARE-MS=Comparison of Alemtuzumab and Rebif® Efficacy in Multiple Sclerosis.

Disability Assessments Through 5 Years

• Expanded Disability Status Scale (EDSS) scores were assessed at baseline and quarterly by raters who were blinded to core study treatment assignment
  – EDSS mean change from baseline
  – 6-Month confirmed disability worsening: ≥1-point EDSS increase (≥1.5 point if baseline EDSS=0)
  – Confirmed disability improvement: ≥1-point EDSS decrease from baseline over 3, 6, or 12 months, assessed in patients with baseline EDSS ≥2.0

Alemtuzumab Retreatment Rate Was Low Through 5 Years

- 7.6% of patients (n=30) received another DMT
- 60% patients received no alemtuzumab retreatment since Month 12
- No reason was provided for 4 cases. Over 5 years, there were 209 retreatments in 158 patients.

Mean EDSS Score Was Stable Through Year 5

- Mean EDSS score was stable through year 5

Confirmed Disability Improvement Was Newly Achieved Through Year 5

- Number at risk is the number of patients who remained on study and who had yet to achieve CDI
- Of patients who entered the extension study, 91% remained on study through Year 5

CDI=confirmed disability improvement.
Most Alemtuzumab-Treated Patients Had Improved or Stable EDSS Scores From Baseline to Year 5

Through Year 5:
- 75% were free from 6-month confirmed disability worsening
- 43% achieved 6-month confirmed disability improvement
  - Of these, 96% were free from 6-month confirmed disability worsening

**Hypothesis: Alemtuzumab Mechanism of Action May Explain Durability of Effect**

1. Selection
 Alemtuzumab binds to CD52, a cell surface antigen present on T and B lymphocytes

2. Depletion
 Depletes circulating T and B lymphocytes

3. Repopulation
 Distinctive repopulation pattern, resulting in a relative increase of cells with memory and regulatory phenotype and a decrease in cells with a pro-inflammatory signature

- Alemtuzumab is administered as 2 courses (5 days at Month 0 and 3 days at Month 12)
- Most patients did not receive any additional treatment (no alemtuzumab retreatment since the initial 2 courses or other DMT)
- EDSS-based disability was improved or stable for most patients over 5 years
- Improvement was evident across all functional systems
- Immunomodulation linked to lymphocyte repopulation may contribute to durability of effect
- Shift from a pro-inflammatory to anti-inflammatory profile
- Based on these findings, alemtuzumab may provide a unique treatment approach with durable efficacy in the absence of continuous treatment for RRMS patients

**Conclusions**

CARE-MS II

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## CARE-MS Study Group and Acknowledgments

| Argentina | Australia | Belgium | Brazil | Canada | Croatia | Czech Republic | Denmark | Finland | France | Germany | Greece | Hungary | Iceland | India | Italy | Japan | Korea | Latvia | Lithuania | Luxembourg | Malaysia | Mexico | Netherlands | Norway | Poland | Portugal | Russia | Serbia | Slovakia | Slovenia | Spain | Sweden | Switzerland | Turkey | United Kingdom | United States (cont) | United States (cont) | United States (cont) |
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| Argentina | Australia | Belgium | Brazil | Canada | Croatia | Czech Republic | Denmark | Finland | France | Germany | Greece | Hungary | Iceland | India | Italy | Japan | Korea | Latvia | Lithuania | Luxembourg | Malaysia | Mexico | Netherlands | Norway | Poland | Portugal | Russia | Serbia | Slovakia | Slovenia | Spain | Sweden | Switzerland | Turkey | United Kingdom | United States (cont) | United States (cont) | United States (cont) |

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