IP017

Baseline Characteristics of Patients Enrolled in LemCourse, a Trial Assessing Effectiveness of a Third Course of Alemtuzumab in RRMS Patients

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OBJECTIVE

- **To present the baseline characteristics of RRMS patients enrolled in LemCourse, a prospective, open-label, phase 3b trial in Germany evaluating the efficacy and safety of a third course of treatment with alemtuzumab**

CONCLUSIONS

- **Patients in the LemCourse trial have mean EDSS scores of 3.1 and received alemtuzumab course 3 19.1 (5.5) months after course 2**
- **LemCourse will provide further evidence of the efficacy and safety of additional alemtuzumab courses in RRMS patients who have already received 2 initial courses**

INTRODUCTION

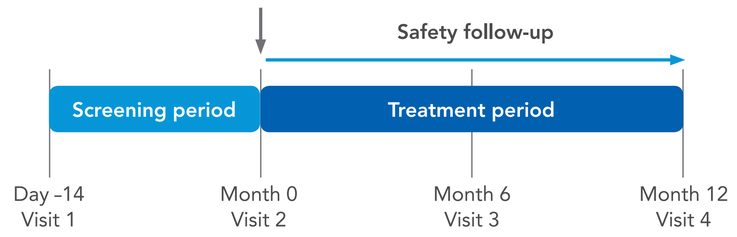
- Alemtuzumab is approved in >70 countries for patients with RRMS, and is administered as 2 courses (course 1: treatment initiation; course 2: 12 months later). Additional courses can be given as needed in the United States (no limit) and European Union (up to 2 additional courses)[1,2]
  - In April 2019, the EMA started an Article 20 referral procedure. The EMA is thereby provisionally restricting the use of alemtuzumab for patients with highly active RRMS, despite a full and adequate course of treatment with at least two other DMTs, or in patients with highly active RRMS where any other DMT is contraindicated or otherwise unsuitable. Data presented in this poster include patients with the label approved in 2013, since data cut off was before the Article 20 procedure started.
  - In the CARE-MS II study (NCT00548405), 2 courses of alemtuzumab demonstrated significantly greater improvements in clinical and MRI outcomes versus SC IFNβ-1a over 2 years[3,4]
- Efficacy was maintained over an additional 5 years in 2 consecutive extension studies (CARE-MS extension [NCT00930553] and the ongoing TOPAZ study [NCT02255656]); 47% of CARE-MS II patients did not receive additional alemtuzumab or other disease-modifying therapy (DMT) after the initial 2 courses[5-9]
  - Over 7 years, 44% of CARE-MS patients received 3 or more courses of alemtuzumab for disease activity[10]
    - Following course 3, relapse rates were significantly reduced, disability was stabilized or improved, and MRI outcomes were significantly improved
  - In clinical trials, adverse events (AEs) in alemtuzumab-treated patients included infusion-associated reactions (IARs), infections, and autoimmune AEs (most commonly thyroid events and, less frequently, immune thrombocytopenia and nephropathies [including anti-glomerular basement membrane disease])[3-9]
  - IARs (predominantly mild or moderate headache, rash, and pyrexia) were experienced by most patients, but decreased with the second treatment course and with each additional course in the group of patients who received additional courses of alemtuzumab
  - Infections occurred in ~60% of alemtuzumab-treated patients in year 1, and declined over time to ~40% in year 5; >95% were mild to moderate with serious infections occurring in 1.0%–1.9% patients per year[11]
  - Thyroid events peaked in the third year after the first alemtuzumab treatment course and declined thereafter; most of these events were mild to moderate
  - Alemtuzumab safety profile in patients who received additional courses was similar to that observed in the overall CARE-MS population and those who did not receive any additional courses[10]
- The effects of alemtuzumab over time may be due to its selective depletion and distinct pattern of repopulation of circulating CD52-expressing T and B lymphocytes[12,13]
  - Following depletion, there is a relative increase in immuno-regulatory T cells and a relative decrease in proinflammatory cytokines, potentially leading to a rebalancing of the immune system; relative increases in immunoregulatory B and natural killer cells may also contribute[7,14-18]
  - The exact mechanism of action of alemtuzumab is not fully elucidated

METHODS

Patients and Assessments

- LemCourse (EudraCT2016-000464-42) is a 1-year, multicenter, single-arm, prospective, open-label, interventional phase 3b study of RRMS patients in Germany, who have previously received 2 courses of alemtuzumab **(Figure 1)**
- Target enrollment: 100 patients at 10–15 study sites in Germany
- Study endpoints include clinical/MRI assessments, PROs, and safety assessments **(Table 1)**

Figure 1. Study Design



a: At the investigator's discretion; b: Starting on the first day of the treatment and continuing for at least 1 month

Table 1. Study Endpoints

Primary endpoints
• Relapse rate in theyear after the third course of alemtuzumab, compared with relapse rate in the year prior to screening • Disability worsening (≥1-point increase in EDSS[19] score)
Secondary endpoints
Efficacy • Percentage of relapse-free patients at Month 12 • Change over time (at Months 6 and 12) in EDSS score • Percentage of patients with active MRI lesions • Change in number of active Gd-enhancing and T2 lesions • Change over time in Symbol Digit Modality Test[20]
Patient-Reported Outcomes • Change over time in Patient-Reported Outcome Indices for Multiple Sclerosis[21] • Change over time in European Quality of Life in 5 Dimensions[22] • Change over time in Work Productivity and Activity Impairment[23]
Safety • AEs/serious AEs/AEs of special interest

Gd: gadolinium.

RESULTS

Patient Demographics and Baseline Characteristics

- LemCourse enrollment is complete
  - 56 patients have been enrolled as of April 4, 2018
- At baseline, LemCourse study patients had mean EDSS scores of 3.1 (1.6) and disease duration of 9.7 (7.1) years **(Table 2)**
- Patients received alemtuzumab course 3 19.1 (5.5) months after course 2
- 87% of patients had an EDSS score ≤4.5 **(Figure 2)**
- Mean (SD) number of relapses in the last 12 months was 1.4 (0.8) **(Table 2)**; 25% of patients had at least 2 relapses prior to alemtuzumab course 3 **(Figure 3)**

Table 2. Demographics and Baseline Characteristics

Parameter	Alemtuzumab (n=56)
Age, years	35.8 (9.2)
Female, n (%)	44 (78.6)
Bodymass index, median (IQR)	23.7 (21.6, 27.4)
EDSS score	3.1 (1.6)
Time from MS diagnosis to alemtuzumab course 3, years	9.7 (7.1)
Time from the 1st MS therapy (other than alemtuzumab) to alemtuzumab course 3, years	9.2 (5.2)
Time from alemtuzumab course 2 to course 3, months	19.1 (5.5)
Number of relapses within 12 months prior to alemtuzumab course 3	1.4 (0.8)
Previous MS therapies	2.7 (1.7)
Types of previous MS therapies, [a]n (%)	
Dimethyl fumarate	8 (16)
Fingolimod	15 (30)
Glatirameracetate	4 (8)
IFNβ	10 (20)
Immunoglobulin	1 (2)
Methylprednisolone	1 (2)
Natalizumab	9 (18)
Siponimod	1 (2)
Teriflunomide	1 (2)
Number of previous MS therapies	
0	6.0 (10.7)
1	8.0 (14.3)
2	12.0 (21.4)
3	13.0 (23.2)
4	10.0 (17.9)
≥5	7.0 (12.5)
Patients who had MRI scans, n (%)	56 (100)
Patients receiving systemic corticosteroids or adrenocorticotrophic hormones, n (%)	7 (12.5)
New Gd-enhancing lesions	1.2 (2.6)
New T2 hyperintense lesions	2.7 (8.1)

a: 50 patients received prior MS therapies.
Values are mean (SD) unless indicated otherwise; IQR: interquartile range.

Figure 2. Distribution of EDSS Scores

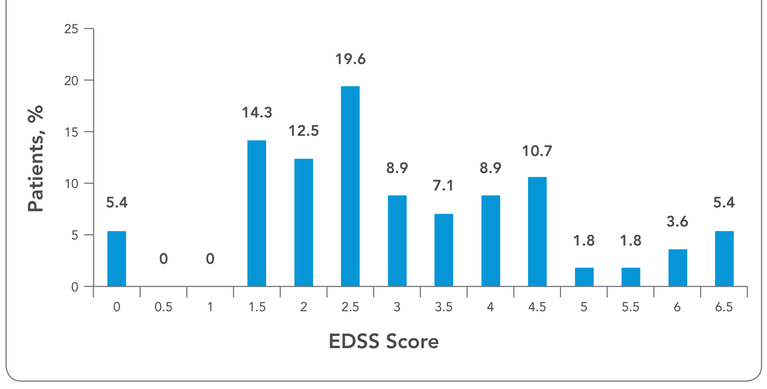
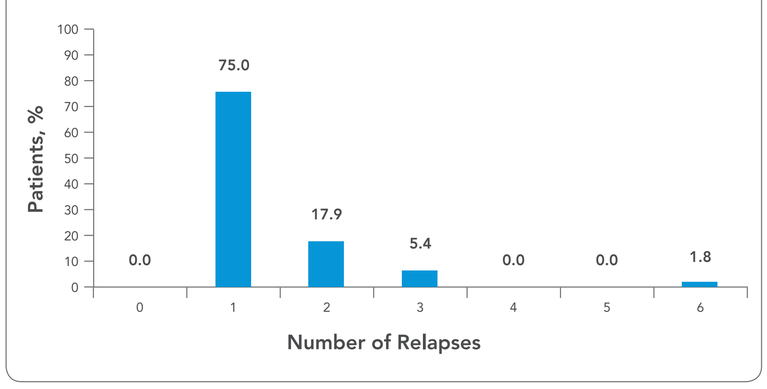


Figure 3. Relapses Prior to Alemtuzumab Course 3



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CARE-MS = Comparison of alemtuzumab and Rebif® Efficacy in Multiple Sclerosis.
TOPAZ = a long-Term follow-up study for multiple sclerOsisPatients who have completed the AlemtuZumab extension study. Rebif® is a registered trademark of EMD Serono, Inc.

Alemtuzumab is approved in >70 countries around the world for treatment of adults with relapsing forms of multiple sclerosis (MS). In April 2019, the EMA has started an Article 20 referral procedure. The EMA is thereby provisionally restricting the use of alemtuzumab in the EU for patients with highly active RRMS, despite a full and adequate course of treatment with at least two other DMTs, or in patients with highly active RRMS where any other DMT is contraindicated or otherwise unsuitable. 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. This material may contain information that is outside of the approved labeling in some countries.

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