Efficacy and Safety of Alemtuzumab Through 9 Years of Follow-up in Patients with Highly Active Disease: Post Hoc Analysis of CARE-MS I and II Patients in the TOPAZ Extension Study

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SUPPLEMENTAL TABLES

Supplementary Table 1 Total follow-up time through Year 9 in CARE-MS I, CARE-MS II, and pooled CARE-MS I and II alemtuzumab-treated HAD patients

	HAD Patients		
	CARE-MS I (*N* = 105)	**CARE-MS II (*N* = 103)**	**Pooled CARE-MS I and II (*N* = 208)**
Total follow-up time, patient-years	927.1	823.2	1750.3
Mean (SD)	8.8 (2.4)	8.0 (2.6)	8.4 (2.6)
Median (range)	9.8 (1.3–11.1)	9.2 (1.1–10.6)	9.5 (1.1–11.1)

CARE-MS Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis, *HAD* highly active disease, *SD* standard deviation

Supplementary Table 2 Efficacy through 9 years in alemtuzumab-treated patients from the pooled CARE-MS I and II studies

	Alemtuzumab-Treated Patients
Parameter	**CARE-MS Overall (Pooled Studies) (*N* = 811)**
Proportion of patients who received neither additional alemtuzumab nor another DMT in the extensions, %	48
Proportion of patients who received additional alemtuzumab, %	49[a]
3 total courses, %	26[a]
4 total courses, %	14[a]
5 total courses, %	6[a]
6 total courses, %	2[a]
7 total courses, %	0.5[a]
8 total courses, %	0.1[a]
ARR over Y3–9 (95 % CI)	0.17 (0.15 to 0.19)
Proportion of patients relapse-free over Y3–9, % (95 % CI)[b]	50 (46 to 54)
Mean EDSS score change over Y0–9 (95 % CI)	0.21 (0.09 to 0.33)
Proportion of patients with improved or stable EDSS over Y0–9[c], %	72 (improved, 22; stable, 51)
Proportion of patients free of 6-Month CDW over Y0–9, % (95 % CI)	64 (60 to 67)
Proportion of patients with 6-Month CDI over Y0–9, % (95 % CI)	45 (41 to 50)
Proportion of patients free of MRI disease activity in Y9, % (95 % CI)[b]	70 (66 to 74)

Proportion of patients with NEDA in Y9, % (95 % CI)[b]	62 (58 to 67)
Proportion of patients with cumulative NEDA over Y3–9, % (95% CI)[b]	18 (14 to 21)
Median BPF change over Y0–9, % (95 % CI)	−1.65 (−1.81 to −1.48)

[a] N=742; [b] CIs were calculated using the Wald method; [c] values may not sum appropriately due to rounding;
Improved EDSS score: ≥ 1.0-point decrease from core study baseline; stable EDSS score: ≤ 0.5-point change in either direction from core study baseline.
CDW: ≥ 1.0-point EDSS increase from core study baseline (or ≥ 1.5 points if baseline EDSS = 0) confirmed over 6 months
CDI: ≥ 1.0-point EDSS decrease from core study baseline confirmed over 6 months (assessed only in patients with baseline EDSS score ≥ 2.0)
Freedom from MRI disease activity: no new Gd-enhancing T1 lesions on current MRI and no new/enlarging T2 hyperintense lesions since last MRI
NEDA: absence of relapse, 6-month CDW, and MRI disease activity
ARR annualized relapse rate, *BPF* brain parenchymal fraction, *CARE-MS* Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis, *CDI* confirmed disability improvement, *CDW* confirmed disability worsening, *CI* confidence interval, *DMT* disease-modifying therapy, *EDSS* Expanded Disability Status Scale, *Gd* gadolinium, *MRI* magnetic resonance imaging, *NEDA* no evidence of disease activity, *Y* year

Supplementary Table 3 AE incidence over Years 0–9 in the overall alemtuzumab-treated populations from CARE-MS I and II

	Alemtuzumab-Treated Patients Over Years 0−9	
AEs, n (%)	**CARE-MS I Overall (*N* = 376)**	**CARE-MS II Overall (*N* = 435)**
Any AE	370 (98.4)	434 (99.8)
Serious AEs	144 (38.3)	195 (44.8)
Infections	313 (83.2)	382 (87.8)
Serious infections	25 (6.6)	52 (12.0)
Autoimmune AEs[a]		
Thyroid AEs	174 (46.3)	190 (43.7)
Serious thyroid AEs	24 (6.4)	23 (5.3)
ITP	6 (1.6)	16 (3.7)
Nephropathies	1 (0.3)	2 (0.5)
Malignancies	9 (2.4)	8 (1.8)
Deaths	7 (1.9)	9 (2.1)

[a] First occurrence of AE within the time period
AE adverse event, *CARE-MS* Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis, *Gd* gadolinium, *ITP* immune thrombocytopenia