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Improvements Across Functional Systems Are Maintained Regardless of Early VS Late Confirmed Disability Improvement: CARE-MS 6-Year Follow-Up

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In CARE-MS studies (NCT00530348; NCT00548405), alemtuzumab showed significant improvement vs SC IFNB-1a in clinical/MRI outcomes over 2 years in patients with RRMS, including higher rates of confirmed disability improvement (CDI). Efficacy was maintained in a 4-year extension (NCT00930553). In CARE-MS II, 71% of patients with CDI achieved improvements in >1 EDSS functional system (FS) score; improvements were seen across all FS. The objective was to assess CDI occurring early/late after alemtuzumab initiation in pooled CARE-MS I and II patients over 6 years, including maintenance of effect and pattern of improvement across FS scores.

Patients received two annual courses of alemtuzumab 12 mg/day (baseline: 5 consecutive days; 12 months later: 3 consecutive days) in the core CARE-MS studies, with as-needed alemtuzumab retreatment/other disease-modifying therapies in the extension. CDI was defined as ≥1-point EDSS decrease confirmed over 6 months. Analyses: percentage of patients with improved/stable EDSS scores from baseline to Y6, and with stable/improved or number of improved FS scores at 6 months post-CDI onset.

171/427 (40%) eligible patients achieved CDI, 60% of whom had EDSS scores that remained improved at Y6; 67% of patients without CDI had stable EDSS scores from baseline–Y6. EDSS improvement/stability at Y6 vs baseline was apparent in patients with early CDI (61%/34%) and late CDI (57%/37%), respectively. At 6 months post-CDI onset, improvement/stability in each FS was observed in 90–100% of patients with early/late CDI; improvement was most frequently in sensory, pyramidal, and cerebellar FS. 74%/18% of CDI patients (early) and 67%/13% (late) achieved improvements in >1 FS/≥4 FS, respectively.

CDI, occurring within the first 2 years or later, was maintained at Y6 in absence of continuous treatment and was associated with improvements across multiple FS, indicating a broad and prolonged effect of alemtuzumab on disability improvement, potentially changing the MS disease course.

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Efficacy and Safety of Ocrelizumab in Patients with Relapsing-Remitting Multiple Sclerosis with a Suboptimal Response to Previous Disease-Modifying Therapies (1-Year Interim Results)

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Patients with relapsing-remitting multiple sclerosis (RRMS) often experience disease activity despite receiving a disease-modifying therapy (DMT). The aim of the prospective, multicentre, single-arm Phase IIIb CASTING study (NCT02861014) is to evaluate the efficacy and safety of ocrelizumab (OCR) in patients with RRMS who had a suboptimal response to an adequate course of 1 or 2 DMTs.

Patients in CASTING (Expanded Disability Status Scale [EDSS] ≤4.0; disease duration ≤10 years; discontinued prior DMT of ≥6 months' duration due to suboptimal disease control) received intravenous OCR 600 mg/24 weeks (first dose, 2 × 300 mg, 14 days apart) for 96 weeks. The proportion of patients with NEDA was measured by an absence of protocol-defined relapses (PDRs), 24-week confirmed disability progression (24W-CDP), T1 gadolinium-enhancing lesions and new/enlarging T2 lesions and were calculated using the modified intent-to-treat population (mITT; patients receiving any dose who discontinued early without a protocol-defined event were imputed as having an event if the treatment discontinuation reason was lack of efficacy or death; others were excluded). MRI outcomes were rebaselined at Week 8 (prespecified analyses).

A total of 680 patients (female, 64%; mean [SD] baseline EDSS score, 2.1 [1.1]; disease duration, 5.0 [2.7] years; pretreated with one DMT, n=411 [60.5%]; pretreated with two DMTs, n=265 [39.5%]) were enrolled in CASTING, most commonly for reasons of relapse on prior DMT, and are included in the mITT population. At Week 48, most patients had NEDA (N=586/674 [86.9%]). Rates of 24W-CDP (N=32/673 [4.8%]), PDR (N=28/674 [4.2%]), T1 gadolinium-enhancing lesions (N=19/673 [2.8%]) and new/enlarging T2 lesions (N=42/673 [6.2%]) were generally low; MRI outcomes were rebaselined at Week 8. The adjusted annualised relapse rate (negative binomial model) was 0.048. A total of 591 patients (86.9%) experienced ≥1 adverse event, and 34 patients (5.0%) experienced ≥1 serious adverse event (includes infusion-related reactions).

Most patients in CASTING had no evidence of MS disease activity. As future data become available and are reported, CASTING will describe additional data on the efficacy and safety of ocrelizumab treatment in patients who had ongoing disease activity while receiving another DMT.

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