

Full title: Proportions of patients with highly active RMS achieving no evidence of disease activity in response to cladribine tablets in CLARITY

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Background: In CLARITY, cladribine tablets (CT) showed efficacy vs placebo (PBO) in a patients with RMS. Patients with high disease activity (HDA) are less likely to attain no evidence of disease activity (NEDA) status.

Objective: Compare CT 3.5mg/kg (CT3.5) vs PBO on the proportion of patients with NEDA in two patient subgroups with HDA at baseline.

Methods: Patients were retrospectively analysed (*post-hoc*) using 2 HDA criteria: 1. high relapse activity (HRA), defined as ≥ 2 relapses during the year before study entry whether on DMD treatment or not 2. HRA plus disease activity on treatment (HRA+DAT) where DAT was defined as ≥ 1 relapse AND ≥ 1 T1 Gd+ or ≥ 9 T2 lesions during the year before the study entry while taking DMDs. Odds ratios (OR) for NEDA status (no qualifying relapses, no 3-month confirmed EDSS progression, no T1 Gd+ lesions and no active T2 lesions) were compared for CT 3.5 vs PBO.

Results: In each HDA subgroup, the proportion meeting individual NEDA criteria was higher with CT3.5. Eg, for HRA 76% of CT3.5-treated patients (n=130) were relapse-free and 84% were T1 Gd+ lesion-free vs 49% and 31%, respectively, for PBO (n=131). For HRA+DAT, 77% were relapse-free and 85% were T1 Gd+ lesion-free with CT 3.5 (n=140) vs 50% and 32%, respectively for PBO (n=149). Composite score: 43.2% of the HRA subgroup and 43.7% of the HRA+DAT subgroup in CT3.5-treated patients achieved NEDA compared with 8.7%, (OR 8.02, 95%CI: 3.93;16.35, $p < 0.0001$) and 9.0% (OR 7.82, 95%CI: 4.03;15.19, $p < 0.0001$) respectively, for PBO. Values were significantly more favourable in the HRA+DAT vs the non-HDA subgroup. For overall CLARITY, the composite NEDA score also favoured CT3.5 over PBO (OR 4.46, 95%CI: 3.18;6.26, $p < 0.0001$).

Conclusions: In patients with active RMS, treatment with CT3.5 significantly increased the proportion of HDA patients achieving NEDA compared with PBO.

The CLARITY study: NCT00213135

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