Title: Durability of No Evidence of Disease Activity-3 (NEDA-3) status in patients with relapsing multiple sclerosis (RMS) receiving Cladribine Tablets 3.5 mg/kg (CT3.5): CLARITY Extension

Short Title (max. 45 characters): Durability of NEDA-3 status in CLARITY Ext

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Introduction: In CLARITY, CT3.5 showed efficacy vs placebo over 2-years in patients with RMS. NEDA-3 status was achieved in significantly more patients receiving CT3.5 than placebo. Efficacy with CT3.5 (CLARITY) was maintained in Years-3/4 (CLARITY Ext) when patients were randomised to placebo after a variable bridging interval (BrI; ≤116 weeks), during which CT3.5 was not administered.

Objective: Determine NEDA-3 status in patients who received CT3.5 in CLARITY followed by placebo (CP3.5) or CT3.5 (CC7) in CLARITY Ext.

Methods: Patients (CP3.5 N=98; CC7 N=186) were retrospectively analysed for NEDA-3 status (no relapse, no 6-month Expanded Disability Status Scale [EDSS] progression, no T1 gadolinium-enhancing or active T2 lesions). BrI between CLARITY and CLARITY Ext was used as a proxy for when patients reached Week 48 of CLARITY Ext. Year 3–4 group: patients with BrI ≤43 weeks (known NEDA status: CP3.5 N=54; CC7 N=98); Year 4–5 group: patients with BrI >43 weeks (known NEDA status: CP3.5 N=40; CC7 N=77). NEDA-3 differences in CP3.5 and CC7 groups were analysed by logistic regression with treatment and BrI as fixed effects.

Results: Year 3–4 group: annual NEDA-3 achieved in 46% (25/54) and 48% (47/98) of the CP3.5 and placebo groups. Year 4–5 group: annual NEDA-3 was observed in 35% (14/40) and 48% (37/77) of the CP3.5 and CC7 groups. Adjusting for BrI length, there was no significant difference between annual NEDA-3 in the CP3.5 (41.5%, 95%CI=32.4–60.0%) and CC7 (48.0%, 95%CI=40.2–64.4%) groups (p=0.31). BrI duration was not a significant variable (p=0.38). Similar patterns were observed when
proportions of patients who were annual relapse-free and annual 6-month EDSS progression-free were examined.

**Conclusions:** Following CT3.5 treatment in CLARITY, NEDA-3 status (analysed *post-hoc*) was sustained in patients up to Week 48 of CLARITY Ext, and BrI was not a significant variable.

The CLARITY study: NCT00213135; The CLARITY Extension study: NCT00641537

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