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**Presentation preference:** Oral or Poster

**Title:** Lymphopenia rates in CLARITY/CLARITY Extension are unrelated to disease activity at baseline

**Short Title:** Lymphopenia rates in CLARITY/CLARITY Ext

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**Introduction:** In CLARITY, patients with high disease activity (HDA) relapsing multiple sclerosis had clinical and magnetic resonance imaging responses to Cladribine Tablets 3.5mg/kg (CT3.5) that were generally better than/comparable to the overall CLARITY population.

**Objectives:** *Post-hoc* analyses to determine lymphopenia rate in patients with HDA in the CLARITY/CLARITY Ext CT3.5 cohort.

**Methods:** Patients were retrospectively analysed using 2 HDA criteria sets: 1.High relapse activity (HRA):  $\geq 2$  relapses in year before study entry, with/without disease modifying drug (DMD) treatment 2.HRA plus disease-activity-on-treatment (DAT):  $\geq 1$  relapse AND  $\geq 1$  T1 gadolinium-enhancing or  $\geq 9$  T2 lesions in year before study entry during treatment with other DMDs. Patients exposed to CT3.5 in Years-1/2 only were the CT3.5 group; the CT7.0 patient group received further courses in Years 3/4. The Adverse Event of Special Interest (AESI) lymphopenia was determined by absolute lymphocyte count (ALC) and lymphopenia from CLARITY/CLARITY Ext.

**Results:** In CT3.5-Year-2, AESIs/100 patient-years were similar in HRA and HRA+DAT subgroups (11.50[N=196];13.09[N=219]), and in corresponding non-HDA groups (14.08[N=489]; 13.46[N=466]). In CT7.0--Year-4 rates were approximately double to CT3.5-Year-2. Mean ALC nadir (x10 /L) for CT3.5-Year-2 HRA and HRA+DAT were 0.73 and 0.72; mean nadirs were 0.69 in corresponding non-HDA subgroups. A similar pattern was seen in CT7.0-Year-4, but with lower nadirs than CT3.5-Year-2. Time to ALC nadir differed slightly between HDA subgroups and was shorter in CT7.0-Year-4 than CT3.5-Year-2. Incidence of Grade-3 lymphopenia for CT3.5-Year-2 was similar between HDA and non-HDA subgroups, and for CT7.0-Year-4 was lower in HDA than non-HDA subgroups. Grade-3 lymphopenia incidence was lower in CT3.5-Year-2 than CT7.0-Year-4. Grade-4 lymphopenia incidence was low in all subgroups.

**Conclusions:** No relevant differences existed between HDA and non-HDA groups regarding incidence of AESI lymphopenia, ALC nadir, and time to ALC nadir. Baseline disease activity appeared unrelated to incidence of lymphopenia during CLARITY/CLARITY Ext.

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

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