Full title: Radiological outcomes with cladribine tablets in high disease activity subgroups of patients with relapsing multiple sclerosis in the CLARITY Study

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Background: The CLARITY study demonstrated efficacy of cladribine tablets (CT) vs placebo (PBO) in patients with RMS. Patients with high disease activity (HDA) are at higher risk of relapses and disability progression.

Objective: Compare CT 3.5mg/kg (CT3.5) vs PBO on magnetic resonance imaging (MRI) outcomes in two patient subgroups with evidence of HDA at baseline.

Methods: CLARITY patients randomised to CT3.5 or PBO were retrospectively analysed (*post-hoc*) using two HDA criteria based on relapse history, prior treatment, and MRI characteristics: 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.

Results: For cumulative new T1 Gd+ lesions, the relative risk ratio (RRR) in the HRA subgroup (0.087, 95%CI:0.052;0.144) was significantly lower for CT3.5 (n=130) vs PBO (n=131, p<0.0001). In the HRA+DAT subgroup, the RRR (0.077, 95%CI:0.046;0.128) favoured CT3.5 (n=140) vs. PBO (n=149, p<0.0001). Risk reductions (91% and 92%, respectively) were similar to the 90% reduction in the overall CLARITY population (0.097, 95%CI:0.070;0.134, p<0.0001). For cumulative active T2 lesions, the RRR also favoured CT3.5 vs. PBO for HRA (0.263, 95%CI:0.180;0.383, p<0.0001) and HRA+DAT (0.254, 95%CI:0.178;0.363, p<0.0001): risk reductions of 74% and 75% reflecting the 73% reduction in the overall population (0.272, 95%CI:0.221;0.335, p<0.0001). The RRR for cumulative combined unique (CU) lesions favoured CT3.5 vs. PBO for HRA (0.212, 95%CI:0.145;0.311, p<0.0001) and HRA+DAT (0.203, 95%CI:0.141;0.291, p<0.0001): risk

reductions of 79% and 80%, reflecting the 77% overall population reduction (0.234, 95%CI:0.190;0.290, p<0.0001). There were no significant interactions between HDA and non-HDA subgroups.

Conclusions In patients with HDA, CT3.5 produced comparable MRI effects to the overall CLARITY population.

The CLARITY study: NCT00213135

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