P515

Efficacy of Cladribine Tablets 3.5 Mg/Kg in High Disease Activity (HDA) Subgroups of Patients with Relapsing Multiple Sclerosis (RMS) in the CLARITY Study

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Background: In the CLARITY study, treatment with cladribine tablets (CTs) showed strong efficacy versus placebo in a large cohort of patients with relapsing multiple sclerosis (RMS) over 2 years. Patients with high disease activity (had) are at higher risk of relapses and disability progression. Here, the effects of CT 3.5 mg/kg (CT3.5) versus placebo were compared in sub-groups of CLARITY patients selected using two HDA definitions.

Methods: CLARITY patients randomised to CT3.5 (N = 433) or placebo (N = 437) were retrospectively analysed using two differ-ent HDA definitions based on relapse history, prior treatment and magnetic resonance imaging (MRI) characteristics. Patients were categorised according to whether they had experienced high relapse activity (HRA; =2 relapses in the previous year) regardless of prior treatment, or HRA plus treatment nonresponse (HRA + TNR; =2 relapses in the previous year, or =1 relapse in previous year while on disease modifying drug (DMD) therapy and =1 T1 Gd+ or =9 T2 lesions).

Results: In the overall CLARITY population, CT3.5 reduced the risk of 6-month confirmed Expanded Disability Status Scale (EDSS) progression versus placebo (hazards ratio (HR) = 0.53, 95% CI: 0.36–0.79). A larger risk reduction for CT3.5 versus pla-cebo was seen (HR = 0.18 each, 95% CI: 0.08–0.44 and 0.07– 0.43) in the HRA subgroup (p = 0.0036 nominal significance vs non-HRA) and the HRA + TNR subgroup (p = 0.0037 signifi-cance vs non-HRA+TNR), indicating greater responsiveness to CT3.5 in patients identified by these criteria. Similar patterns were observed for time to 3-month EDSS progression. ARR was lower with CT3.5 than placebo in the overall population (relative risk (RR) = 0.42, 95% CI: 0.33–0.52), and even lower with HRA (RR = 0.32, 95% CI: 0.22–0.47) and HRA + TNR (RR = 0.33, 95% CI: 0.23–0.48; each p < 0.0001 vs placebo). Strong treatment effects on radiological markers were observed in each HDA subgroup.

Conclusion: In CLARITY, patients identified by HDA criteria showed clinical and MRI responses to CT3.5 that were generally better than, or at least comparable with, the overall CLARITY population.