Objective: Cladribine is activated preferentially in lymphocytes, resulting in targeted and sustained immunomodulation, providing the rationale for its use as a short-course annual multiple sclerosis (MS) treatment. We assessed the safety and tolerability of cladribine tablets versus placebo over 96 weeks in the CLARITY (CLAdRIbine tablets Treating multiple sclerosis orally) study. CLARITY is the largest placebo-controlled trial to be completed in relapsing-remitting MS (RRMS).

Methods: Patients with RRMS (McDonald criteria) were randomized 1:1:1 to receive cladribine tablets (cumulative dose 5.25 or 3.5 mg/kg) or matching placebo. Cladribine tablets were given in short courses (once daily for 4–5 days) in 2 or 4 consecutive months (28-day periods) in the first 48 weeks, then at weeks 48 and 52 (both groups). Safety and tolerability assessments were conducted throughout the study. Results were previously presented at the Congress of the European Committee for Treatment and Research in Multiple Sclerosis in 2009.

Results: Of 456, 433, and 437 patients randomized to cladribine 5.25 or 3.5 mg/kg or placebo, 454, 430, and 435 received the study drug and were evaluable for safety analysis, with 86.2%, 91.2%, and 86.3% successfully completing full-course treatment, respectively. Lymphopenia occurred more commonly with cladribine treatment (26.7%) than with placebo (1.8%), as anticipated based on its mechanism of action. Similar proportions of patients developed infections during the study (48.3% vs. 42.5%), with 20 patients treated with cladribine developing dermatomal herpes zoster (2.3%). Three isolated malignancies were reported during the study in the cladribine 3.5 mg/kg group (ovarian and pancreatic carcinomas and a malignant melanoma), and a precancerous cervical in situ case (stage 0) was reported in the 5.25 mg/kg group. A choriocarcinoma was reported in post-study surveillance. There were two deaths in each treatment group, including one in the 5.25 mg/kg group secondary to reactivation of latent tuberculosis infection.

Conclusions: Together with the efficacy data (reported elsewhere), the results suggest that cladribine tablets may provide an important new option in MS therapy. Longer-term safety of cladribine tablets is being further investigated in a 96-week CLARITY EXTENSION study.

Keywords: disease-modifying treatment in MS