

Title: Long-term Disease Stability Assessed by the Expanded Disability Status Scale in Patients Treated with Cladribine Tablets in the CLARITY and CLARITY Extension Studies

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Short title to be displayed on app: Cladribine Tablets: Long-term EDSS Stability

Background: Treatment with cladribine tablets 10mg (cumulative dose 3.5mg/kg [CT3.5] over 2 years) in CLARITY and CLARITY Extension reduced relapse rate and slowed disability progression versus placebo in patients with relapsing remitting multiple sclerosis (RRMS). This *post hoc* analysis evaluated long-term disease stability assessed by the Expanded Disability Status Scale (EDSS) after treatment with CT3.5 in patients with RRMS enrolled in CLARITY and CLARITY Extension.

Methods: Patients randomised to CT3.5 in CLARITY and then to placebo in CLARITY Extension, with ≥ 1 post-baseline EDSS measurement, were included (CP3.5; n=98). EDSS score over-time (from CLARITY randomisation to end of follow-up in CLARITY Extension, including the bridging interval between studies) was assessed at 6-monthly intervals, and separately time to 3- and 6-month confirmed EDSS score progression from CLARITY baseline. EDSS score worsening/improvement in each year was defined as any increase/decrease in minimum EDSS score at 6-monthly intervals; all other cases were classified as stable. An increase or decrease was defined as an EDSS score change of 1, 1.5 or 0.5 points at baseline EDSS ≤ 4.5 , 0, ≥ 5.0 respectively.

Results: Five years post-CLARITY baseline, median EDSS remained stable compared with baseline values. Median EDSS score (95% confidence interval [CI]) for patients in the CP3.5 group was 2.5 (2.0-3.5) compared with 3.0 (2.5-3.5) at baseline. In each 12-month period, EDSS score stability was observed in $>50\%$ of patients, improvement in 21-30% and worsening in 0-25%. During Year 5 in the CP3.5 group, EDSS stability was observed in 53.9% of patients, improvement in 21.3% and worsening in 24.7%. Less than 30% of patients reach 3- or 6-month confirmed EDSS progression by Year 5.

Conclusions: EDSS score was stable up to 5 years post-CLARITY baseline for the CP3.5 group. Between 20% and 30% of patients demonstrated improvement in EDSS score versus baseline each year.

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