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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INTRODUCTION

- The CLARITY study demonstrated that treatment with cladribine tablets 10 mg (cumulative dose 5.5 mg/kg [CT5.5]) significantly reduced relapse rates and showed disease progression versus placebo in patients with multiple sclerosis (MS) and relapsing-remitting MS (RRMS) patients.
- The CLARITY Extension study showed that treatment with cladribine tablets for 2 years followed by treatment with placebo for 2 years produced similar clinical benefits in 4 years of cladribine tablets treatment but with lower incidence of grade 3/4 lymphopenia.
- Disease stability and MS can be assessed through the Expanded Disability Status Scale (EDSS). The scale for neurological impairment ranges from 0–10 where a higher score indicates a greater degree of disability and therefore progression of the disease.

OBJECTIVE

- To evaluate post hoc long-term disease stability assessed by the EDSS score after treatment with CT3.5 in patients with RRMS enrolled in CLARITY and CLARITY Extension.

METHODS

Eligibility and Endpoints
- Patients enrolled in the CLARITY Extension who were randomised to CT3.5 in CLARITY with at least one postbaseline EDSS measurement were included for analysis. CLARITY Extension was a post-published study, aiming to extend the bridging interval (median duration 43 weeks) between studies where no cladribine tablets were administered.
- Two treatment groups were assessed (Figure 1):
  - CT3.5: CT3.5 followed by placebo in CLARITY Extension.
  - CC7: CT3.5 followed by CT3.5 in CLARITY Extension.
- Endpoints:
  - EDSS scores over time at 6-monthly intervals, from CLARITY randomisation to end of follow-up in CLARITY Extension, including bridging interval between studies.
  - Patients whose EDSS scores are shown for CT3.5 are not represented in the values of CLARITY Extension.
- No EDSS scores were retrospectively collected during the bridging interval between CLARITY and CLARITY Extension.
- Time up to 3- and 6-month confirmed EDSS progression from CLARITY Extension.
- EDSS score improvement or worsening each year was defined as any increase or decrease in minimum EDSS score at 6-monthly intervals. All other cases were classified as stable.
- An increase or decrease was defined as EDSS score changes of:
  - At least 1.5 points, if baseline EDSS score 0.
  - At least 1 point, if baseline EDSS score 1–4.5.
  - At least 0.5 points, if baseline EDSS score ≥ 5.

RESULTS

EDSS Over Time
- Five years after CLARITY baseline, including variable bridging interval, median EDSS score remained stable compared to baseline values for both groups (Figure 2).
- Median EDSS score remained between 2.0–3.0 up to 60 months in the CP3.5 group (n = 89).
- Median change in EDSS score was 0 points up to 60 months.
- In the CC7 group (n = 126), median EDSS score ranged between 2.0–3.5 up to 60 months.
- Median (95% CI) EDSS score for patients in the CP3.5 group at 5 years was 2.5 (2.0–3.0) compared with 2.3 (2.0–3.0) at baseline.
- Similar results were observed for both groups when split by a variable bridging interval of 0 or ≥ 43 weeks.

Figure 4. Time to 3- (a) and 6-Month (b) Confirmed EDSS Progression

Figure 2. EDSS Score Over Time in Patients Treated with CP3.5 and CC7

- Median EDSS score remained stable for up to 5 years post-CLARITY baseline in both the CP3.5 and CC7 treatment groups.
- Over 50% of patients had stable EDSS score up to 5 years.
- Less than 30% of subjects reached 3- or 6-month confirmed EDSS progression at 5 years.

CONCLUSIONS

- Median EDSS score remained stable for up to 5 years post-CLARITY baseline in both the CP3.5 and CC7 treatment groups.
- Over 50% of patients had stable EDSS score up to 5 years.
- Less than 30% of subjects reached 3- or 6-month confirmed EDSS progression at 5 years.

REFERENCES


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