CONTINUOUS VERSUS NON-CONTINUOUS LONG-TERM, SUBCUTANEOUS, INTERFERON BETA-1A TREATMENT IN RELAPSING–REMITTING MULTIPLE SCLEROSIS

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Introduction

- The Prevention of Relapses and disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis (PRISMS) study showed that interferon (IFN) beta-1a, 22 or 44 mcg subcutaneously (sc) three times weekly (tiw), was effective at reducing relapses and delaying disability progression, compared with placebo, in patients with relapsing–remitting multiple sclerosis (RRMS).[1]
- Data from long-term follow up (LTFU; up to 8 years) confirmed the efficacy of sc IFN beta-1a,[2] and demonstrated a greater therapeutic effect in patients originally randomized to the higher dose compared with those whose treatment had been delayed by 2 years.
- The effect of treatment interruption on clinical outcomes is unknown. The objective of this post-hoc exploratory analysis was to assess long-term clinical efficacy outcomes in the LTFU cohort of the PRISMS study; specifically, in patients originally randomized to IFN beta-1a, 44 mcg sc tiw. Outcomes in patients who received treatment continuously were compared with those who had some treatment interruptions.

Methods

Study design

- The PRISMS study comprised the phases outlined below.
  - In the initial 2-year, double-blind phase, patients with RRMS were randomized to receive IFN beta-1a, 22 or 44 mcg sc tiw, or placebo.
  - Patients originally randomized to placebo were then re-randomized to IFN beta-1a, 22 mcg or 44 mcg sc tiw, for 2 additional years (years 3–4).
  - On study completion, all patients were given the choice of continuing to receive blinded or open-label treatment during years 5–6.
  - Beyond year 6, patients could continue on any or no disease-modifying drug (DMD).
- Patients were eligible for enrollment in the LTFU study if they had been randomized in the original PRISMS study.
- Patients had a single LTFU assessment close to the seventh or eighth anniversary of their baseline visit.
  - The assessment included neurologic evaluation, as well as a retrospective review of data collected since the final 4-year assessment.
  - Progression to secondary progressive MS (SPMS) was defined as a progressive increase in disability of at least 1 point on the Expanded Disability Status Scale (EDSS; 0.5 points if baseline EDSS was ≥6) not associated with a relapse.[2]

Post-hoc exploratory analysis

- In this post-hoc exploratory analysis, patients who were randomized on study day 1 to IFN beta-1a, 44 mcg sc tiw, were divided into two groups:
  - 'continuous'; patients randomized on study day 1 to IFN beta-1a, 44 mcg sc tiw, who remained on that dose until LTFU, with no interruptions (no other DMDs taken)
  - 'non-continuous'; patients randomized on study day 1 to IFN beta-1a, 44 mcg sc tiw, who had some medication interruptions (irrespective of other DMDs received).
- Clinical outcomes were assessed in the two groups. Only descriptive statistics were applied.

Results

- Of the184 patients originally randomized at study day 1 of the PRISMS study to IFN beta-1a, 44 mcg sc tiw, 136 (74%) participated in the LTFU visit.
  - A total of 45 patients were in the continuous treatment group; 91 patients were in the non-continuous treatment group.
  - Ten patients in the non-continuous group received treatment with other DMDs.
- Mean (standard deviation) cumulative dose exposure was 49.4 (2.6) and 34.0 (13.5) mg/patient in the continuous and non-continuous groups, respectively.
- Patients in the continuous group had a lower mean annualized relapse rate than those in the non-continuous group, from baseline until LTFU, and over each study period analyzed (**Figure 1**).
- The proportion of patients who were free from relapses from baseline until LTFU was similar between groups (**Figure 2**).
- From baseline until LTFU, a lower proportion of patients in the continuous group converted to SPMS, compared with the non-continuous group (**Figure 3**).

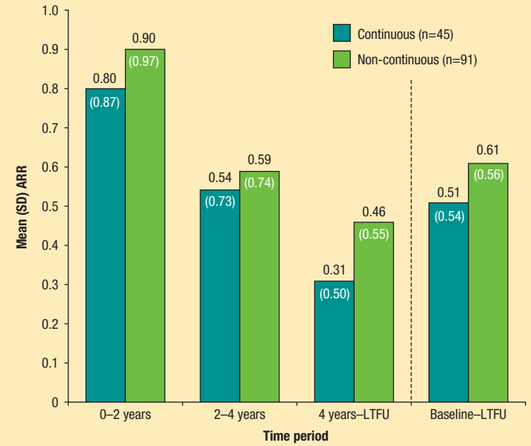

Figure 1. Mean (standard deviation [SD]) annualized relapse rate (ARR) in patients originally randomized to interferon beta-1a, 44 mcg sc tiw, and without (continuous) or with (non-continuous) treatment interruptions (baseline to long-term follow up [LTFU]).

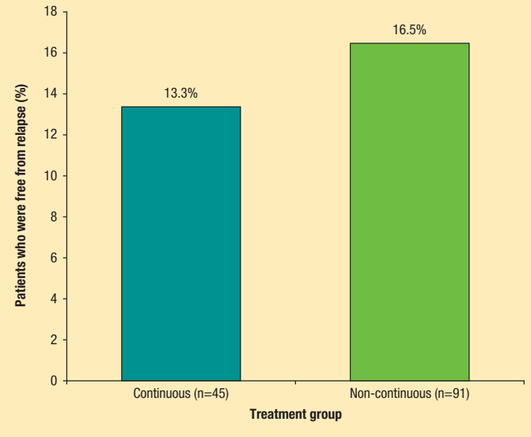

Figure 2. Proportion of patients who were free from relapses among patients originally randomized to interferon beta-1a, 44 mcg sc tiw, and without (continuous) or with (non-continuous) treatment interruptions (baseline to long-term follow up).

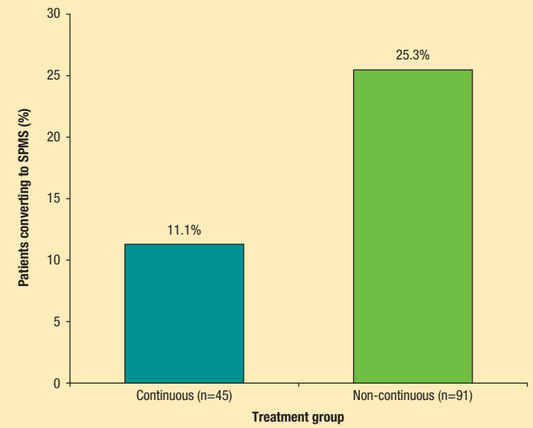

Figure 3. Proportion of patients converting to secondary progressive multiple sclerosis (SPMS) among patients originally randomized to interferon beta-1a, 44 mcg sc tiw, and without (continuous) or with (non-continuous) treatment interruptions (baseline to long-term follow up).

Conclusions

- This exploratory analysis showed that patients with RRMS receiving continuous treatment with IFN beta-1a, 44 mcg sc tiw, for up to 8 years, experienced better clinical outcomes over the long term than those who had treatment interruptions.
- This suggests that superior efficacy may be experienced by patients who adhere to treatment and avoid interruptions over the long term
  - Further studies are warranted to investigate the effect of treatment interruption on efficacy outcomes.

References

1. PRISMS Study Group. Lancet 1998;352:1498–504.
2. Kappos L et al. Neurology 2006;67:944–53.
3. PRISMS Study Group and the University of British Columbia MS/MRI Analysis Group. Neurology 2001;56:1628–36.

Acknowledgments

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