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 (twi), was effective at reducing relapses and delaying disability progression, compared with placebo, in patients with relapsing-remitting multiple sclerosis (RRMS). Data from long-term follow-up (LTFU; up to 8 years) confirmed the efficacy of sc IFN beta-1a, 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 twi. 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 twi, or placebo. – Patients originally randomized to placebo were then re-randomized to IFN beta-1a, 22 mcg or 44 mcg sc twi, for 2 additional years (years 3–6). – 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.

Results

Of the 184 patients originally randomized at study day 1 of the PRISMS study to IFN beta-1a, 44 mcg sc twi, 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).

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 twi, were divided into two groups: – ‘continuous’; patients randomized on study day 1 to IFN beta-1a, 44 mcg sc twi, 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 twi, who had some medication interruptions (irrespective of other DMDs received).

Clinical outcomes were assessed in the two groups. Only descriptive statistics were applied.

Conclusions
This exploratory analysis showed that patients with RRMS receiving continuous treatment with IFN beta-1a, 44 mcg sc twi, 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

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