LONG-TERM SUBCUTANEOUS INTERFERON BETA-1A TREATMENT IN RELAPSING–REMITTING MULTIPLE SCLEROSIS: CUMULATIVE DOSE EFFECTS

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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 associated with significant benefits in terms of relapses, disability progression, and magnetic resonance imaging (MRI) lesion burden and activity measures compared with placebo in patients with relapsing–remitting multiple sclerosis (RRMS).1

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 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. – Patients were eligible to participate 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 4-year assessment.

Post-hoc exploratory analysis

Patient data from the three original study arms were pooled and ranked into quartiles from lowest to highest estimated cumulative dose of sc IFN beta-1a received (from baseline to LTFU). – Clinical and MRI outcomes were assessed in the minimum (lowest quartile, MIN) and maximum (highest quartile, MAX) dose groups. – Only descriptive statistics were applied.

Results

Of 566 patients originally randomized in the PRISMS study, 178 (31.8%) were lost to follow up: 382 (68.2%) participated in the LTFU visit. Of these 382 patients, 123 patients were originally randomized to IFN beta-1a 22 mcg, 136 to IFN beta-1a 44 mcg, and 123 to placebo.

Cumulative dose

Patients in the MAX dose group had a lower mean annual relapse rate (ARR) than those in the MIN dose group, from baseline to LTFU, and over each study period analyzed (Figure 3).

In addition, the proportion of patients who were free from relapses was greater (Figure 2), and the proportion of patients who converted to secondary progressive MS (SPMS) was lower (Figure 4) in the MAX dose group compared with the MIN dose group from baseline to LTFU.

Conclusions

Results from exploratory analyses of data from the PRISMS LTFU study demonstrated that patients with RRMS exposed to the highest cumulative dose of sc IFN beta-1a experienced greater benefits on clinical and MRI outcomes than those with lower cumulative dose exposure, for up to 8 years.

Greater benefits were also seen in patients with the highest cumulative exposure to sc IFN beta-1a.

These findings support the importance of treating early with high-dose, high-frequency sc IFN beta-1a and maintaining therapy over the long term.

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References