The BETAPAEDIC Study: Assessment of Safety, Tolerability, Clinical Effectiveness and Cognition in Juvenile Relapsing-Remitting MS Patients Treated With Interferon Beta-1b

**INTRODUCTION**

The incidence of multiple sclerosis (MS) in children and adolescents is increasing. Interferon beta-1b (IFN-B-1b, Betaseron®) has a favourable safety profile and is known to reduce relapse rate (RR) in patients ≥18 years of age with relapsing-remitting MS (RRMS). Retrospective studies with low numbers have indicated a similar safety profile in juvenile MS.

**Objective:** The BETAPAEDIC study is the first prospective, international, multicentre, non-interventional, post-authorisation safety study to assess the safety and tolerability of IFN-B-1b in juvenile MS patients, measuring clinical activity and magnetic resonance imaging disease parameters. Determining the neuropsychological profile, such as interferon beta-1b (IFN-B-1b; Betaseron®), in children have often been extrapolated from data collected in adults.1,4,12

However, small retrospective studies and case reports in paediatric populations14-20 indicate that IFN-B-1b has a favourable safety profile—similar to that seen in adults1,21—and may reduce relapse rate and delay disease progression.

**Information on the safety and efficacy of IFN-B-1b in children and adolescents is limited.**

**The BETAPAEDIC study—**the first prospective, international, multicentre, non-interventional, post-authorisation safety study—has thus been undertaken to assess the safety and tolerability profile of IFN-B-1b in adolescents with RRMS.

**Study Design**

The BETAPAEDIC study seeks to recruit 100 treatment-naïve patients aged 12–16 years old who were diagnosed with RRMS by core diagnostic criteria and scheduled to receive IFN-B-1b. Patients will be recruited from neurologic/ paediatric centres across Europe between January 2010 and March 2012 (Table 1). Patients will be treated at the discretion of their attending physicians with the standard IFN-B-1b dose (250 μg), injected subcutaneously every other day.

Patients will be examined every 6 months for up to 2 years (Table 2).

**Introduction**

- Approximately 3-10% of all patients with multiple sclerosis (MS) experience symptom onset before the age of 18 years.1 Although juvenile MS is becoming increasingly recognised, its exact prevalence is unknown.

- Juvenile MS patients present almost exclusively (97%) with the relapsing-remitting form of the disease.1 RRMS.

- Children with MS face unique problems related to the severity and potential long-term consequences of the disease, which include physical disability, cognitive impairment2 and psychological impact.3

- Among children with paediatric MS, cognitive impairment is hypothesised to occur in the domains of processing speed,4 concentration,5 verbal working memory,6 abstract reasoning7 and visual-motor integration.

- Compared to patients with adult-onset disease, paediatric MS patients take approximately 10 years longer from diagnosis to reach second primary progressive MS and irreversible MS disease.8

- Although paediatric MS may progress more slowly, disease milestones are reached at a younger age, with paediatric MS patients converting to SPMS at a 10-year younger median age relative to adult MS patients.9

- In adults, early treatment has been shown to delay conversion to clinically definite MS (COM)10 and to positively affect clinical and magnetic resonance imaging (MRI) aspects of the disease.11,12

- In light of the benefits shown in adults, the International Pediatric MS Study Group recommends early treatment for children with paediatric MS.13

**Evaluations**

**Clinical effectiveness will be assessed by annualised RR and Expanded Disability Status Scale score progression.**

**Fatigue will be measured by the Fatigue Severity Scale.**

**Standard Progressive Matrices (SPM) will be used to assess intellectual ability.**

**Neuropsychological function will be evaluated by four sub-tests:**

- vocabulary, block design, digit span and spelling from the Wechsler Intelligence Scale for Children—fourth edition (WISC-IV®).

- Visual-motor integration and verbal memory, spatial analysis, visual-motor integration, visual perception, motor coordination, intelligence and vocabulary.

- Disease course

- MRI outcomes

**Outcomes Assessment**

For clinical outcomes, the proportion of relapse-free patients, the time to first relapse and annualised RR will be reported.

**Neuropsychological outcomes will include the change in total scores from baseline to each visit.** Neuropsychological outcomes will also be compared with age-matched normative values.

**Correlation analyses between neuropsychological outcomes and the following will be performed:**

- Processing speed, concentration, verbal working memory, spatial analysis, visual-motor integration, visual perception, motor coordination, intelligence and vocabulary

- Disease course

- MRI outcomes

**Perspective**

The BETAPAEDIC study is expected to illuminate the effectiveness and safety profile of IFN-B-1b in children and adolescents and to illustrate the level of cognitive dysfunction in patients with juvenile MS.

**The BETAPAEDIC study should also help to confirm findings from retrospective-scale studies, which showed a similar safety profile for IFN-B-1b in juveniles and adults.1,2,13**

**Potential correlations between disease-related variables, fatigue and neurocognitive outcomes may provide insights into the factors that modulate disease progression with betasheets with juvenile MS.**

As with adults, it is hoped that early treatment with IFN-B-1b will translate into favourable long-term outcomes in children and adolescents with MS. However, prolonged follow-up studies are needed to determine such effects and whether the long-term safety profile observed in adults1,12 is recapitulated in patients with rates (RR) and delay disease progression.13

**REFERENCES**


