Interferon beta-1b 16-Year Long-Term Follow-Up Study: MRI Outcomes

ABSTRACT

Background: The interferon beta-1b (IFNB; Betaseron®) pivotal study demonstrated efficacy, safety and tolerability of IFNB-1b in patients with relapsing-remitting multiple sclerosis, including a persistent beneficial effect on MRI lesion burden over 5 years. The 10-Year Long-Term Follow-Up (10-Year LTF) study is hypothesis generating, with the aim to assess the long-term treatment effects of IFNB-1b on clinical and MRI outcomes.

Methods: The 16-Year LTF is a multicentre, open-label, observational study with longitudinal data collected from patients from all 11 centres who participated in the original pivotal trial. MRI scans were analysed at one single centre and MRI outcome measures assessed included T2 burden of disease (BOD), normalised brain volume (NBV), T2/BOD, gadolinium (Gd)-enhancing lesions (Gd), T1 hypointense lesions, ‘black holes’ (BH) and cervical C2 area.

Results: 310 of the original 327 patients have been identified (83.4%), 192 patients underwent MRI studies (BOD, NBV – 187 patients, Gd – 184 patients, BH – 181 patients and C2A – 181 patients). An in-depth analysis was performed between T2/BOD, NBV, BH, C2A, correlation with disability and the stratified groups. The continuous suppression of Gd-enhancing lesions in patients on IFNB-1b treatment within the first 60 days compared with patients who discontinued therapy prior to age 140 suggested a sustained treatment effect over 14 years of therapy.

Conclusions: Although significant differences in the treatment to analysis were not observed, preliminary results indicate that the changes in the different MRI measures over time in the whole cohort are in line with expected clinical progression. Assessment of the C2A for the first time in a multicentre setting, results are consistent with the brain measurements, even though this value was collected on a smaller number of patients, mainly for technical reasons and availability at specific centres.

Introduction

Background: The original trial to assess the efficacy of IFNB-1b (Betaseron®) in the first randomised, placebo-controlled, double-blind, dose-ranging study to be performed in the USA and Canada from 1988–1993.

1. The IFNB Multiple Sclerosis Study Group and The University of British Columbia MS/MRI Study Group and the IFNB Multiple Sclerosis Study Group.

2. IFNB Multiple Sclerosis Study Group.

3. Paty DW, Li DKB, the UBC MS/MRI Study Group and the IFNB Multiple Sclerosis Study Group.

4. Li DKB, Paty DW, Clodic S, the IFNB Multiple Sclerosis Study Group.


The current analysis of the original cohort of the pivotal IFNB-1b trial, and constitutes the longest follow-up for any disease-modifying therapy in MS. The 16-Year LTF is a multicentre, open label, observational study with longitudinal data collected from patients from all 11 centres who participated in the original pivotal trial. MRI scans were analysed at one single centre and MRI outcome measures assessed included T2 burden of disease (BOD), normalised brain volume (NBV), T2/BOD, gadolinium (Gd)-enhancing lesions (Gd), T1 hypointense lesions, ‘black holes’ (BH) and cervical C2 area.

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Objectives of the 16-Year LTF Study: MRI

To: determine the long-term effects of IFNB-1b treatment on MRI measures.

Study Design

• Multicentre, open-label, observational study of patients with relapsing forms of MS who participated in the pivotal IFNB-1b trial from all 11 centres. MRI outcome measures were assessed at a single centre and the MRI analyses were presented.

• 10-Year LTF: 11 centres, 166 patients, of which 108 patients were on active treatment for at least 10 years. MRI outcome measures were assessed at a single centre.

• 16-Year LTF: 11 centres, 168 patients, of which 108 patients were on active treatment for at least 14 years. MRI outcome measures were assessed at a single centre.

• T2 BOD was estimated as the total volume (in mm3) of T2 hyperintense lesions on axial PD/T2-weighted images.

• NBV was calculated as the median normalised brain volume.

• Gd-enhancing lesions were counted as lesions with Gadolinium (Gd) enhancement on post-injection T1-weighted images.

• T1 BH were estimated as the total volume (in mm3) of T1 hypointense lesions on axial T1-weighted images.

• C2A was calculated as cervical C2 area in millimetres squared.

• 10-Year LTF and 16-Year LTF: MRI scans were done at one single visit together with the clinical examination.

• Median normalised brain volume values were lower in patients with greater disability.

• The area of T1 hypointense lesions (black holes) according to the duration of treatment effects on suppression of Gd-enhancing lesions for at least 30 days. An analysis of lasting effects of up to 90 days since discontinuation was planned, but identified no patients in this group, therefore, this finding could not be performed.

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• This was the first multicentre trial assessing cervical C2 area and the scans were obtained from a smaller group of patients than the other MRI parameters. Reduction in cervical C2 area showed a correlation with greater disability.

• This study is supported by Schering AG, Berlin, Germany.

• The majority of the original study patients (88.2%) could still be located from the 11 participating study centres and 293 are alive while 35 have been identified as deceased. Patient disposition in the 16-year follow up section will evaluate the current MRI status of the patients and will be published separately.

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