Abstract No. 416

Administration of IFN beta 1a in the evening ameliorates flu-like symptoms in the early phase of treatment in multiple sclerosis: data from RELIEF study

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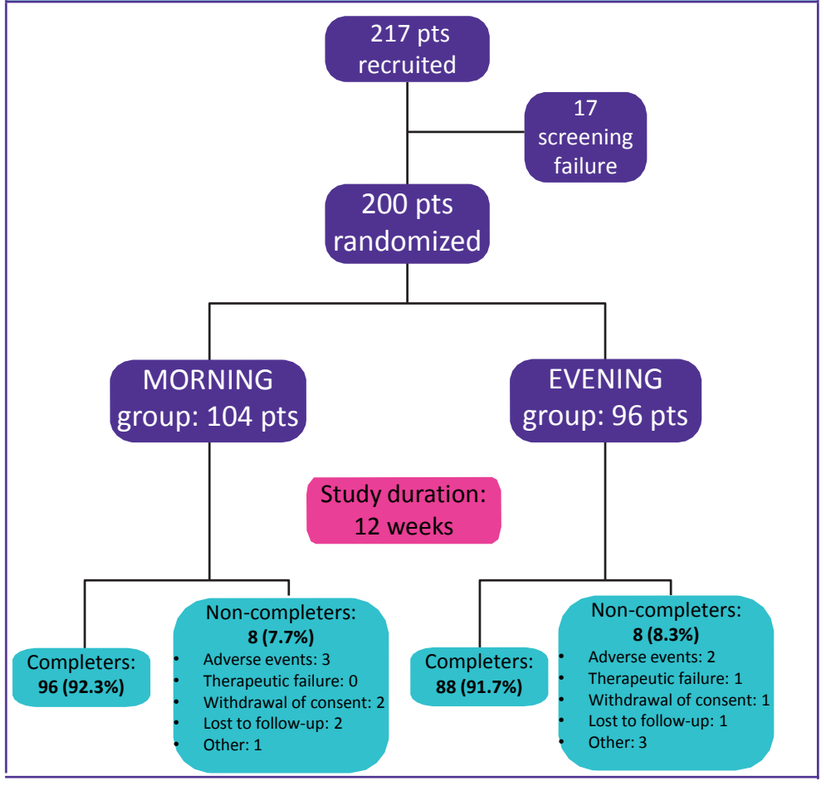
INTRODUCTION

- Flu-like symptoms (FLS) are among the most common adverse effects in the use of interferon (IFN) beta in multiple sclerosis (MS)
- Although it is recommended that IFN-beta injections should be administered in the evening, previous studies had reported that morning injections could reduce severity of FLS due to a decrease in interleukin-6 secretion [1], [2]

OBJECTIVE

- The primary objective was to evaluate whether administration of subcutaneous IFN beta 1a (Rebif) in the morning or in the evening may affect the severity of FLS and patient-perceived symptoms in subjects with relapsing MS over a period of 12 weeks
- The primary endpoint was to assess the severity of FLS, as measured by items 13-16 of the Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ), in subjects injecting Rebif 44 mcg thrice weekly in the morning compared to the evening administration
- The main secondary objectives were aimed to assess the longitudinal changes in injection site reactions and global side-effects, changes in anxiety symptoms, fatigue symptoms, sleep disorders and quality of life in the morning group compared to the evening and to assess adherence to treatment

Figure 1. Patients disposition

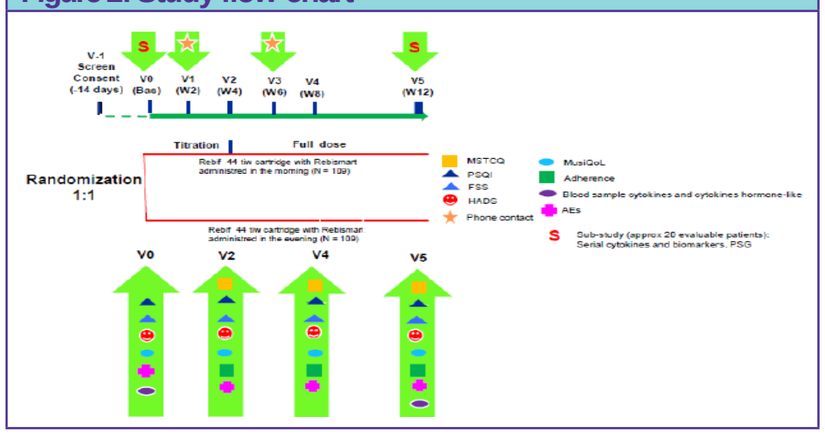


METHODS

Study Design

RELIEF was a multicenter, open-label, prospective, randomized study

Figure 2. Study flow-chart



Evaluations (Figure 2)

- MSTCQ
- Hospital Anxiety and Depression Scale (HADS)
- Fatigue Severity Scale (FSS)
- Pittsburgh Sleep Quality Index (PSQI)
- Multiple Sclerosis International Quality of Life
- Adherence to treatment using RebiSmart®
- Circulating levels of cytokines

RESULTS

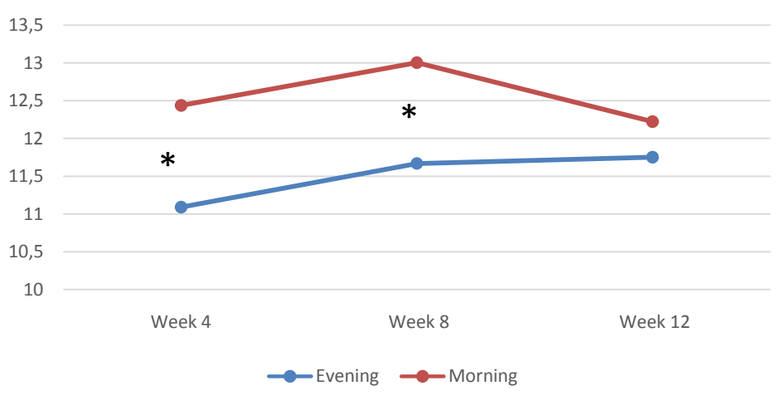
Study population

217 patients were included in the study at 29 Italian sites and 200 were randomized. Of these, 104 patients (76 females and 28 males, mean age 37.3 ± 10.1 years, mean baseline EDSS 1.89) were randomized to administer IFN beta 1a in the morning and 96 patients (62 females and 34 males, mean age 34.9 ± 10.8 years, mean baseline EDSS 1.87) in the evening **(Figure 1)**.

Main Analysis results (Figure 3)

- **4 weeks** after starting therapy, patients in the morning group reported a significantly higher score in items 13-16 of MSTCQ when compared to the evening group (difference between adjusted means: 1.35, CI 0.35-2.35, p=0.008)
- The difference was still significant after **8 weeks** (difference between adjusted means: 1.34, CI 0.35-2.32, p=0.008)
- The difference was no longer significant at the end of the observation period of **12 weeks** of therapy (difference between adjusted means: 0.47, CI -0.52-1.46, p=0.35)

Figure 3. MSTCQ: FLS scores evening *vs* morning



* p value for adjusted mean difference Morning - Evening < 0.01.
Analysis is based on a linear mixed model for repeated measures with FLS score at each visit as dependent variable, while treatment group, visit (Week 4, Week 8, Week 12), treatment by visit interaction as fixed factors of the model and patient as random effect

Secondary Analysis

Adherence to study medication

Mean (±SD) cumulative adherence recorded by RebiSmart® at week 12 was 98.6 ± 9.8 % in the morning group and 98.1 ± 10.0 % in the evening group.
(Adherence = 100 X number of injections administered/number of expected injections)

Safety results

No new safety or tolerability concerns were identified following treatment with Rebif 44 mcg tiw in the morning or evening group for 12 weeks

CONCLUSIONS

- Based on data from RELIEF study, evening injections led to an improvement of IFN beta-related flu-like symptoms in the very initial phase of treatment; with the continuation of the therapy this advantage tended to decrease
- Therefore to start the injection of IFN beta in the evening could lead to a better management of FLS in patients with MS, while in the continuation of therapy the time of administration could be decided according to patient's lifestyle and preference

REFERENCES

1. Kümpfel T, Schwan M, Pollmächer T, Yassouridis A, Uhr M, Trenkwalder C, Weber F. Time of interferon-beta 1a injection and duration of treatment affect clinical side effects and acute changes of plasma hormone and cytokine levels in multiple sclerosis patients. Mult Scler (2007);13(9):1138-45

2. Nadjar Y, Coutelas E, Prouteau P, Panzer F, Paquet D, Saint-Val C, Créange A. Injection of interferon-beta in the morning decreases flu-like syndrome in many patients with multiple sclerosis. Clin Neurol Neurosurg (2011);113(4):316-322

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DISCLOSURES

Prof. Patti served on the scientific advisory board for Teva, Biogen-Idec, Bayer-Schering, Novartis, and has received honoraria as a speaker for Teva, Biogen, Merck-Serono, Bayer-Schering, Genzyme/Sanofi, and Novartis.

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