ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 10/21/2013

ClinicalTrials.gov ID: NCT00735007

Study Identification

Unique Protocol ID:	28733
Brief Title:	12-week Study to Evaluate RebiSmart™ Suitability for Self Injection in Relapsing Multiple Sclerosis.
Official Title:	International, Multicenter, Single-arm, Open-label, 12-week Phase IIIb Study to Evaluate RebiSmart™ Suitability for Self Injection of Rebif® New Formulation (RNF) in Multidose Cartridges in Patients With Relapsing Form of Multiple Sclerosis (RMS)
Secondary IDs:	

Study Status

Record Verification:	October 2013
Overall Status:	Completed
Study Start:	July 2008
Primary Completion:	January 2009 [Actual]
Study Completion:	

Sponsor/Collaborators

Sponsor:	EMD Serono
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: BB- IND 5371 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration Sweden: Medical Products Agency Italy: Ethics Committee Germany: Federal Institute for Drugs and Medical Devices Spain: Ethics Committee Canada: Health Canada European Union: European Medicines Agency

Study Description

Brief Summary: The Electronic Device - The RebiSmart™ is an electronic injection device that is being studied for the delivery of Merck Serono's Rebif® New Formulation. The RebiSmart™ device is a stand-alone hand-held device with internal power supply. It is used for subcutaneous (under the skin) injections with single-use sterile disposable needles. The device will be kept in a storage box and placed in the refrigerator after each use.

The key features of the RebiSmart™ are as follows:

- Battery powered electromechanical automatic injector;
- Automatic needle attachment and detachment;
- Hidden needle before and after injection;
- Injection can only be initiated by pressing the injection button when in contact with the skin;
- Automatic needle insertion and injection of the preset dose into the subcutaneous (under the skin) tissue;
- Adjustable injection comfort parameters: Injection depth, needle insertion speed, medication injection speed and time that the needle remains in the skin ;
- Cartridges with 3 doses of Rebif® New Formulation; and
- Several other electronic functions including history (date and time) of cartridge changes and injections.

The Study Drug - Rebif® New Formulation (RNF) Rebif® is a medicine that is part of a family of proteins called interferon beta-1a (IFN-β-1a) molecules that play an important role in the immune system and help limit the damage that occurs with

multiple sclerosis (MS). The interferon in Rebif® is like your body's own natural human interferon, but is made outside the body by a process called "recombinant DNA technology". Merck Serono International S.A. (the maker of Rebif®) has recently updated the method to make Rebif®, and it is referred to as Rebif® New Formulation (RNF).

For the purpose of this study, the form of Rebif® New Formulation (RNF) will differ slightly from the one you currently receive. RNF will be supplied in pre-filled cartridges containing three doses of 44mcg / 0.5 ml IFN-β-1a. This is the amount required for you to administer during the course of one full week of treatment. The dosage of RNF 44mcg is injected under the skin three times per week. The RebiSmart™ device will be provided for the administration of RNF. RNF should be administered, if possible, at the same time (preferably in the late afternoon or evening) on the same three days (e.g. Monday, Wednesday, and Friday), with at least 48 hours break between each administration. You will be asked to record the time and date of each injection in the diary cards provided. You will be taught how to properly use the device to inject the medication. You will also be reminded to rotate injection sites and advised on the importance of avoiding already inflamed areas for future injections.

The goals of this research trial are:

- To evaluate if the electronic device can be used (if it is suitable) by MS patients performing self-injections of Rebif® New Formulation.
- To determine MS patients overall satisfaction of the new RebiSmart™ device by determining their ease in using it, how often side effects happen (flu-like symptoms, injection site reactions and any other overall injection issues) that they may experience while on the trial. This will be done by completion of the Patient User Trial Questionnaire and the Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ).
- To evaluate specific features of the RebiSmart™ device from the answers MS patients provide in the User Trial Questionnaire. The MS patient and the person who will trains them on the proper use of the device will complete this questionnaire.

Detailed Description:

Conditions

Conditions: Multiple Sclerosis

Keywords: Multiple Sclerosis

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 3

Intervention Model: Single Group Assignment

Number of Arms: 1

Masking: Open Label

Allocation: N/A

Endpoint Classification: Safety/Efficacy Study

Enrollment: 106 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: Rebif® New Formulation (RNF) using RebiSmartTM RNF 44 mg, 3 times a week by subcutaneous injection.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 65 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Males and females between 18 and 65 years of age, inclusive
- Female subjects must be neither pregnant nor breast-feeding and must lack child-bearing potential, as defined by either:
  - Post-menopausal or surgically sterile, or
  - Using a highly effective method of contraception for the duration of the study. This is defined as a method that result in a low failure rate (i.e., less than 1% per year) when used consistently and correctly, and includes for instance implants, injectables, combined oral contraceptives, intra-uterine device (IUD)s, sexual abstinence or vasectomised partner.
- Have RMS according to the revised McDonald Criteria 2005
- Have disease duration for at least 3 months
- Are currently receiving RNF 44 mcg sc by Rebiject IITM (RII) tiw and have been consistently on therapy for a minimum of 6 weeks prior to Screening

Exclusion Criteria:

- Have any disease other than MS that could better explain his/her signs and symptoms
- Receive any other injectable medications on a regular basis during the week prior to the screening period or throughout the duration of the study. The administration of a single injection for treatment or prophylaxis of a condition unrelated to the patient's MS or the patient's RNF therapy (e.g., influenza or pneumococcus vaccination) will be acceptable

- Receive any MS therapy other than Rebif / RNF (e.g., other disease-modifying drug [DMD]s: immunomodulatory , immunosuppressive agents or combination therapy) within 12 months prior to study enrolment or at any time during the study
- Receive oral or systemic corticosteroids or adrenocorticotrophic hormone (ACTH) within 30 days prior to SD1
- Have inadequate liver function, defined by a alanine aminotransferase (ALT) > 3 x upper limit of normal (ULN), or alkaline phosphatase > 2 x ULN, or total bilirubin > 2 x ULN if associated with any elevation of ALT or alkaline phosphatase
- Have inadequate bone marrow reserve, defined as a white blood cell count less than 0.5 x lower limit of normal
- Have moderate to severe renal impairment
- History of any chronic pain syndrome
- Any visual or physical impairment that precludes the subject self-injecting the treatment using the RebiSmartä

Contacts/Locations

Study Officials: Elisabetta Verdun di Cantogno, MD
Study Director
Merck Serono International, S.A., an affiliate of Merck KGaA, Darmstadt, Germany

Locations: United States, Massachusetts
US Local Medical Information
Rockland, Massachusetts, United States, 02370

Canada
Canada, Local Medical Information
Ontario, British Columbia, Quebec, Canada

Germany
Germany, Local Medical Information
Hamburg, Ulm, Berlin, Erbach, Germany

Italy
Italy, Local Medical Information
Chieti & Roma, Italy, Italy

Spain
Spain, Local Medical Information
Barcelona & Madrid, Spain, Spain

Sweden
Sweden, Local Medical Information
Sweden, Sweden

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	First Patient First Visit : 30 July 2008 Last Patient Last Visit: 27 January 2009 15 specialist neurology centres in 6 countries: Canada (3 sites), Germany(4 sites) , Italy (2 sites) , Spain(3 sites), Sweden (1 sites), USA(2 sites)

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Overall Study

	RebiSmart for Self-injection
Started	106
Completed	101
Not Completed	5
Adverse Event	4
Protocol Violation	1

Baseline Characteristics

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Baseline Measures

	RebiSmart for Self-injection
Number of Participants	106
Age, Categorical [units: participants]	
<=18 years	0
Between 18 and 65 years	106
>=65 years	0
Age, Continuous [units: years] Mean (Standard Deviation)	41.7 (9.3)
Gender, Male/Female [units: participants]	
Female	65
Male	41
Region of Enrollment [units: participants]	
United States	21
Canada	16
Spain	24
Germany	26
Italy	14
Sweden	5
Diastolic blood pressure [units: mmHg] Mean (Standard Deviation)	75.5 (10.1)
Heart rate [units: beats/min] Mean (Standard Deviation)	74.9 (9.0)
Temperature [units: °C] Mean (Standard Deviation)	36.40 (0.43)
Thyroid Peroxidase antibody [units: IU/ml] Mean (Standard Deviation)	220 (181.9)

	RebiSmart for Self-injection
Systolic Blood Pressure [units: mmHg] Mean (Standard Deviation)	118.4 (13.1)
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Flu Like Symptom (FLS) Score items 13-16 [1] [units: units on a scale] Mean (Standard Deviation)	9.5 (3.7)
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Global Side Effects Score items 21-23 [2] [units: units on a scale] Mean (Standard Deviation)	4.8 (1.7)
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Site Reaction Score items 17-20 [3] [units: units on a scale] Mean (Standard Deviation)	11.1 (3.3)

[1] Intention to treat population. MSTCQ FLS Score items 13-16 has a best possible score of 4 and a worst possible score of 20.

[2] Intention to treat population. MSTCQ Global Side Effects Score items 21-23 has a best possible score of 15 and a worst possible score of 3.

[3] Intention to treat population. MSTCQ Injection Site Reaction Score items 17-20 has a best possible score of 4 and a worst possible score of 20.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	The Number of Subjects Rating the Suitability of RebiSmart at the End of 12-week Treatment Period for Self-injecting Rebif® New Formulation (RNF).
Measure Description	RebiSmart was evaluated as "very suitable or suitable"; "a little suitable"; or "not suitable at all" for self-injecting RNF. The Patient User Trial Questionnaire (UTQ) provides confidence in the ability to evaluate the suitability of the device and ease of understanding the different features of the RebiSmart during the training session and the overall subject impression of the injection administration. Subjects completed the Patient UTQ at Study Day1, Week4, and Week12. The Trainer User UTQ provides confidence in the ability to evaluate the suitability of the RebiSmart by the trainer.

Time Frame	End of 12 week treatment period
Safety Issue?	No

Analysis Population Description
4 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	102
The Number of Subjects Rating the Suitability of RebiSmart at the End of 12-week Treatment Period for Self-injecting Rebif® New Formulation (RNF). [units: participants]	
suitable or very suitable	73
a little suitable	21
not suitable at all	8

2. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Flu Like Symptom (FLS) Score Items 13-16 at End Week 4
Measure Description	Intention to treat population. MSTCQ FLS Score items 13-16 has a best possible score of 4 and a worst possible score of 20.
Time Frame	at the end of week 4 of treatment
Safety Issue?	No

Analysis Population Description
3 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	103
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Flu Like Symptom (FLS) Score Items 13-16 at End Week 4 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	8.8 (3.9)

3. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Flu Like Symptom (FLS) Score Items 13-16 at End Week 8
Measure Description	Intention to treat population. MSTCQ FLS Score items 13-16 has a best possible score of 4 and a worst possible score of 20.
Time Frame	at the end of week 8 of treatment
Safety Issue?	No

Analysis Population Description

6 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	100
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Flu Like Symptom (FLS) Score Items 13-16 at End Week 8 [units: MSTCQ Score (units on a scale)]	8.8 (3.8)

	RebiSmart for Self-injection
Mean (Standard Deviation)	

4. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Flu Like Symptom (FLS) Score Items 13-16 at End Week 12
Measure Description	Intention to treat population. MSTCQ FLS Score items 13-16 has a best possible score of 4 and a worst possible score of 20.
Time Frame	at the end of week 12 of treatment
Safety Issue?	No

Analysis Population Description
Intention to treat population

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	106
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Flu Like Symptom (FLS) Score Items 13-16 at End Week 12 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	9.0 (3.8)

5. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Site Reaction Score Items 17-20 at End Week 4
Measure Description	Intention to treat population. MSTCQ InjectionSite Reaction Score items 17-20 has a best possible score of 4 and a worst possible score of 20.

Time Frame	at the end of week 4 of treatment
Safety Issue?	No

Analysis Population Description
3 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	103
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Site Reaction Score Items 17-20 at End Week 4 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	11.4 (3.2)

6. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Site Reaction Score Items 17-20 at End Week 8
Measure Description	Intention to treat population. MSTCQ InjectionSite Reaction Score items 17-20 has a best possible score of 4 and a worst possible score of 20.
Time Frame	at the end of week 8 of treatment
Safety Issue?	No

Analysis Population Description
6 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	100
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Site Reaction Score Items 17-20 at End Week 8 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	11.3 (3.5)

7. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Site Reaction Score Items 17-20 at End Week 12
Measure Description	Intention to treat population. MSTCQ InjectionSite Reaction Score items 17-20 has a best possible score of 4 and a worst possible score of 20.
Time Frame	at the end of week 12 of treatment
Safety Issue?	No

Analysis Population Description

Intention to treat population

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	106
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Site Reaction Score Items 17-20 at End Week 12 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	11.4 (3.4)

8. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Global Side Effects Score Items 21-23 at End Week 4
Measure Description	Intention to treat population. MSTCQ Global Side Effects Score items 21-23 has a best possible score of 15 and a worst possible score of 3.
Time Frame	at the end of week 4 of treatment
Safety Issue?	No

Analysis Population Description

3 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	103
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Global Side Effects Score Items 21-23 at End Week 4 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	5.5 (2.4)

9. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Global Side Effects Score Items 21-23 at End Week 8
Measure Description	Intention to treat population. MSTCQ Global Side Effects Score items 21-23 has a best possible score of 15 and a worst possible score of 3.
Time Frame	at the end of week 8 of treatment
Safety Issue?	No

Analysis Population Description

6 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	100
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Global Side Effects Score Items 21-23 at End Week 8 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	5.2 (2.2)

10. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Global Side Effects Score Items 21-23 at End Week 12
Measure Description	Intention to treat population. MSTCQ Global Side Effects Score items 21-23 has a best possible score of 15 and a worst possible score of 3.
Time Frame	at the end of week 12 of treatment
Safety Issue?	No

Analysis Population Description

Intention to treat population

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	106
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Global Side Effects Score Items 21-23 at End Week 12 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	5.6 (2.6)

11. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Issues Score Item 34 at End Week 4
Measure Description	Intention to treat population. MSTCQ Injection Issues Score item 34: +5 is the best possible score (much better), -5 is the worst possible score (much worse), zero is neutral (no change)
Time Frame	at the end of week 4 of treatment
Safety Issue?	No

Analysis Population Description

3 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	103
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Issues Score Item 34 at End Week 4 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	0.2 (2.5)

12. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Issues Score Item 34 at End Week 8
Measure Description	Intention to treat population. MSTCQ Injection Issues Score item 34: +5 is the best possible score (much better), -5 is the worst possible score (much worse), zero is neutral (no change)
Time Frame	at the end of week 8 of treatment
Safety Issue?	No

Analysis Population Description

5 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	101
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Issues Score Item 34 at End Week 8 [units: MSTCQ Score (units on a scale)] Mean (Standard Deviation)	0.1 (1.9)

13. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Issues Score Item 34 at End Week 12
Measure Description	Intention to treat population. MSTCQ Injection Issues Score item 34: +5 is the best possible score (much better), -5 is the worst possible score (much worse), zero is neutral (no change)
Time Frame	at the end of week 12 of treatment
Safety Issue?	No

Analysis Population Description

Intention to treat population

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	106
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Injection Issues Score Item 34 at End Week 12 [units: MSTCQ Score (units on a scale)]	0.2 (2.0)

	RebiSmart for Self-injection
Mean (Standard Deviation)	

14. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Benefit Item 35 at End Week 4
Measure Description	Intention to treat population. MSTCQ Injection Issues Score item 35 - Most important benefit of the RebiSmart injection system: Fewer injection site reactions; less injection pain; fewer flu-like symptoms; fewer physical side effects; or overall convenience.
Time Frame	at the end of week 4 of treatment
Safety Issue?	No

Analysis Population Description

21 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	85
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Benefit Item 35 at End Week 4 [units: participants]	
fewer injection site reactions	13
less injection pain	17
fewer flu-like symptoms	9
fewer physical side effects	5
overall convenience	50

15. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Benefit Item 35 at End Week 8
Measure Description	Intention to treat population. MSTCQ Injection Issues Score item 35 - Most important benefit of the RebiSmart injection system: Fewer injection site reactions; less injection pain; fewer flu-like symptoms; fewer physical side effects; or overall convenience.
Time Frame	at the end of week 8 of treatment
Safety Issue?	No

Analysis Population Description

21 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	85
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Benefit Item 35 at End Week 8 [units: participants]	
fewer injection site reactions	8
less injection pain	13
fewer flu-like symptoms	6
fewer physical side effects	8
overall convenience	59

16. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Benefit Item 35 at End Week 12
Measure Description	Intention to treat population. MSTCQ Injection Issues Score item 35 - Most important benefit of the RebiSmart injection system: Fewer injection site reactions; less injection pain; fewer flu-like symptoms; fewer physical side effects; or overall convenience.
Time Frame	at the end of week 12 of treatment

Safety Issue?	No

Analysis Population Description
21 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	85
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Benefit Item 35 at End Week 12 [units: participants]	
fewer injection site reactions	6
less injection pain	11
fewer flu-like symptoms	6
fewer physical side effects	5
overall convenience	63

17. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Scale Item 37 at End Week 4
Measure Description	Intention to treat population. MSTCQ Pain Rating Scale item 37. Visual Analogue Scale 0mm (No pain) to 100mm (Worst possible pain)
Time Frame	at the end of week 4 of treatment
Safety Issue?	No

Analysis Population Description
4 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	102
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Scale Item 37 at End Week 4 [units: mm (on a scale)] Mean (Standard Deviation)	30.2 (24.6)

18. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Scale Item 37 at End Week 8
Measure Description	Intention to treat population. MSTCQ Pain Rating Scale item 37. Visual Analogue Scale 0mm (No pain) to 100mm (Worst possible pain)
Time Frame	at the end of week 8 of treatment
Safety Issue?	No

Analysis Population Description

5 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	101
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Scale Item 37 at End Week 8 [units: mm (on a scale)] Mean (Standard Deviation)	30.8 (24.9)

19. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Scale Item 37 at End Week 12
Measure Description	Intention to treat population. MSTCQ Pain Rating Scale item 37. Visual Analogue Scale 0mm (No pain) to 100mm (Worst possible pain)
Time Frame	at the end of week 12 of treatment
Safety Issue?	No

Analysis Population Description

Intention to treat population

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	106
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Scale Item 37 at End Week 12 [units: mm (on a scale)] Mean (Standard Deviation)	30.0 (25.1)

20. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Grade Item 38 at End Week 4
Measure Description	Intention to treat population. MSTCQ Pain Rating Grade item 38. Rated as No pain; Mild; Discomforting; Distressing; or Horrible Excruciating
Time Frame	at the end of week 4 of treatment
Safety Issue?	No

Analysis Population Description

5 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	101
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Grade Item 38 at End Week 4 [units: participants]	
No pain	18
Mild	44
Discomforting	26
Distressing	11
Horrible Excruciating	2

21. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Grade Item 38 at End Week 8
Measure Description	Intention to treat population. MSTCQ Pain Rating Grade item 38. Rated as No pain; Mild; Discomforting; Distressing; or Horrible Excruciating
Time Frame	at the end of week 8 of treatment
Safety Issue?	No

Analysis Population Description

5 subjects with missing values

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	101
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Grade Item 38 at End Week 8 [units: participants]	
No pain	17
Mild	46
Discomforting	25
Distressing	12
Horrible Excruciating	1

22. Secondary Outcome Measure:

Measure Title	Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Grade Item 38 at End Week 12
Measure Description	Intention to treat population. MSTCQ Pain Rating Grade item 38. Rated as No pain; Mild; Discomforting; Distressing; or Horrible Excruciating
Time Frame	at the end of week 12 of treatment
Safety Issue?	No

Analysis Population Description

Intention to treat population

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Measured Values

	RebiSmart for Self-injection
Number of Participants Analyzed	106
Multiple Sclerosis Treatment Concern Questionnaire (MSTCQ) Pain Rating Grade Item 38 at End Week 12 [units: participants]	

	RebiSmart for Self-injection
No pain	18
Mild	42
Discomforting	31
Distressing	11
Horrible Excruciating	4

23. Secondary Outcome Measure:

Measure Title	The Incidence of Predefined Injection Site Reactions, MSTCQ Scores, Side Effects, McGill Pain Questionnaire, Visual Analog Scale, and Rating of Pain Regarding Injection Pain Following RNF Administration With RebiSmart at 12-week Treatment Period.
Measure Description	Information on these outcomes is shown separately above, apart from information on the incidence of injection site related adverse events which is shown in the Adverse Events section
Time Frame	at the end of weeks 4, 8, and 12 of treatment
Safety Issue?	No

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	The timeframe over which adverse events were collected was during the 12-week treatment period.
Additional Description	Intent to treat population. The Other Adverse Events table shows all adverse events occuring a frequency equal to or greater than the reporting threshold.

Reporting Groups

	Description
RebiSmart for Self-injection	Rebif New Formulation 44 mg, 3 times a week by subcutaneous injection.

Serious Adverse Events

	RebiSmart for Self-injection	
	Affected/At Risk (%)	# Events
Total	6/106 (5.66%)	
Cardiac disorders		
Myocardial disorders [A] *	1/106 (0.94%)	1
General disorders		
Adverse drug reaction [A] *	1/106 (0.94%)	1
Hepatobiliary disorders		
Biliary colic [A] *	1/106 (0.94%)	1
Infections and infestations		
Breast infection [A] *	1/106 (0.94%)	1
Injury, poisoning and procedural complications		
Seroma [A] *	1/106 (0.94%)	1
Vascular disorders		
Hypertensive crisis [A] *	1/106 (0.94%)	1

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	RebiSmart for Self-injection	
	Affected/At Risk (%)	# Events
Total	67/106 (63.21%)	
General disorders		
Adverse drug reaction [A] *	1/106 (0.94%)	1
Chills [A] *	3/106 (2.83%)	7
Fatigue [A] *	1/106 (0.94%)	1

	RebiSmart for Self-injection	
	Affected/At Risk (%)	# Events
Impaired healing [A] *	1/106 (0.94%)	1
Infuenza like illness [A] *	22/106 (20.75%)	54
Injection site erythema [A] *	2/106 (1.89%)	2
Injection site extravasation [A] *	1/106 (0.94%)	1
Injection site irritation [A] *	2/106 (1.89%)	2
Injection site pain [A] *	3/106 (2.83%)	3
Pyrexia [A] *	2/106 (1.89%)	2
Infections and infestations		
Borrelia infection [A] *	1/106 (0.94%)	1
Breast infection [A] *	1/106 (0.94%)	1
Bronchitis [A] *	3/106 (2.83%)	3
Gastroenteritis [A] *	2/106 (1.89%)	2
Influenza [A] *	4/106 (3.77%)	4
Nasopharyngitis [A] *	10/106 (9.43%)	15
Otitis media acute [A] *	1/106 (0.94%)	1
Pharyngitis [A] *	1/106 (0.94%)	1
Respiratory tract infection [A] *	1/106 (0.94%)	1
Upper respiratory tract infection [A] *	5/106 (4.72%)	6
Vulvovaginal mycotic infection [A] *	1/106 (0.94%)	1
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	2/106 (1.89%)	2
Back pain [A] *	1/106 (0.94%)	1

	RebiSmart for Self-injection	
	Affected/At Risk (%)	# Events
Muscle spasms [A] *	1/106 (0.94%)	3
Myalgia [A] *	3/106 (2.83%)	5
Neck pain [A] *	1/106 (0.94%)	1
Pain in extremity [A] *	2/106 (1.89%)	2
Nervous system disorders		
Facial palsy [A] *	1/106 (0.94%)	1
Headache [A] *	12/106 (11.32%)	25
Monoparesis [A] *	1/106 (0.94%)	1
Neuralgia [A] *	1/106 (0.94%)	1
Syncope vasovagal [A] *	1/106 (0.94%)	1

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

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