ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 01/27/2014

ClinicalTrials.gov ID: NCT01034579

## Study Identification

| | |
|---|---|
| Unique Protocol ID: | EMR200136_023 |
| Brief Title: | The REbif® vs Glatiramer Acetate in Relapsing Multiple Sclerosis Pharmacogenetics Trial ( REGARD-PGx ) |
| Official Title: | A Multinational, Multicenter, Single Blood Sampling Exploratory Pharmacogenetic Study of the REGARD (the REbif® vs Glatiramer Acetate in Relapsing MS Disease) Trial |
| Secondary IDs: | |

## Study Status

| | |
|---|---|
| Record Verification: | January 2014 |
| Overall Status: | Completed |
| Study Start: | February 2010 |
| Primary Completion: | November 2010 [Actual] |
| Study Completion: | November 2010 [Actual] |

## Sponsor/Collaborators

| | |
|---|---|
| Sponsor: | EMD Serono |
| Responsible Party: | Sponsor |
| Collaborators: | |

## Oversight

| | |
|---|---|
| FDA Regulated?: | No |
| IND/IDE Protocol?: | No |

| | |
|---|---|
| Review Board: | Approval Status: Pending<br>Board Name: USA, Western Institutional Review Board<br>Board Affiliation: No Affiliation<br>Phone: 1-800-562-4789<br>Email: clientservices@wirb.com |
| Data Monitoring?: | No |
| Plan to Share Data?: | |
| Oversight Authorities: | Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica<br>Canada: Health Canada<br>France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)<br>Ireland: Irish Medicines Board<br>Italy: National Monitoring Centre for Clinical Trials - Ministry of Health<br>Netherlands: The Central Committee on Research Involving Human Subjects (CCMO)<br>Spain: Spanish Agency of Medicines<br>United Kingdom: Medicines and Healthcare Products Regulatory Agency<br>Russia: Ministry of Health of the Russian Federation |

## Study Description

| | |
|---|---|
| Brief Summary: | This study, REbif® vs Glatiramer acetate in relapsing multiple sclerosis (MS) disease - pharmacogenetic(s) (REGARD-PGx) is a single blood sampling exploratory pharmacogenetic study of the REGARD trial.<br><br>The aim of this trial is to provide additional data on the factors influencing interferon (IFN) beta response.<br><br>This is a Phase 4 trial involving subjects who previously participated in the REGARD trial. To address the trial objectives, a single visit follow-up trial will be performed during which a blood sample will be collected. |
| Detailed Description: | |

## Conditions

| | |
|---|---|
| Conditions: | Relapsing Multiple Sclerosis |
| Keywords: | Biomarkers<br>Genetic markers |

## Study Design

| | |
|---|---|
| Study Type: | Interventional |
| Primary Purpose: | Other |
| Study Phase: | Phase 4 |

| | |
|---|---|
| Intervention Model: | Parallel Assignment |
| Number of Arms: | 2 |
| Masking: | Open Label |
| Allocation: | Non-Randomized |
| Endpoint Classification: | N/A |
| Enrollment: | 324 [Actual] |

## Arms and Interventions

| Arms | Assigned Interventions |
|---|---|
| Rebif® Cohort | Blood sampling<br>Subjects who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study will be enrolled in this retrospective cohort study wherein single blood sampling will be performed for pharmacogenetic markers analysis. |
| Copaxone® Cohort | Blood sampling<br>Subjects who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study will be enrolled in this retrospective cohort study wherein single blood sampling will be performed for pharmacogenetic markers analysis. |

## Outcome Measures

[See Results Section.]

## Eligibility

| | |
|---|---|
| Minimum Age: | 18 Years |
| Maximum Age: | |
| Gender: | Both |
| Accepts Healthy Volunteers?: | No |
| Criteria: | Inclusion Criteria: |

- Was randomized in the REGARD 24735 study
- Is willing and able to comply with the protocol
- Has given written informed consent before performing any trial-related activities

Exclusion Criteria:

- Is unwilling or unable to participate in the study
- Is already included in the initial REGARD 24735 PGx sub-study

## Contacts/Locations

Study Officials: Elisabetta Verdun di Cantogno, MD
Study Director
Merck Serono S.A - Geneva

Locations: United States, Massachusetts
Please Contact U.S. Medical Information Located in
Rockland, Massachusetts, United States

## References

Citations:

Links:

Study Data/Documents:

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# Study Results

## Participant Flow

| | |
|---|---|
| Pre-Assignment Details | Of the 758 participants randomized and treated in study 24735 (NCT00078338), 326 were enrolled in EMR200136_023 (NCT01034579) out of which 2 participants, who had participated in initial pharmacogenetics (PGx) sub-study, were found to be ineligible and therefore, evaluable population for EMR200136_023 (NCT01034579) comprised of 324 participants. |

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

| | Description |
|---|---|
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Overall Study

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| Started | 158 | 166 |
| Completed | 158 | 166 |
| Not Completed | 0 | 0 |

## Baseline Characteristics

Analysis Population Description

Evaluable population included all randomized participants who had received at least 1 dose of Rebif® or Copaxone® in 24735 (NCT00078338) and not participated in the initial PGx sub-study and provided consent to take part in this EMR200136_023 study (NCT01034579).

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial pharmacogenetics (PGx) sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Baseline Measures

| | Rebif® Cohort | Copaxone® Cohort | Total |
|---|---|---|---|
| Number of Participants | 158 | 166 | 324 |
| Age, Continuous<br>[units: years]<br>Mean (Standard Deviation) | 36.4 (9.5) | 37.4 (9.5) | 36.9 (9.5) |
| Gender, Male/Female<br>[units: participants] | | | |
| Female | 99 | 119 | 218 |

| | Rebif® Cohort | Copaxone® Cohort | Total |
|---|---|---|---|
| Male | 59 | 47 | 106 |

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Percentage of Responders as Defined by Single Nucleotide Polymorphism (SNP) Markers |
| Measure Description | A responder was defined as a participant with no multiple sclerosis (MS) relapse and no Expanded Disability Status Scale (EDSS) progression during 96 weeks in 24735 (NCT00078338). All responders were categorized on the basis of following six SNP markers: SNP1, SNP2, SNP3, SNP4, SNP5, and SNP6. Two types of variables were possible for each SNP marker: two-level genotype-based or three-level allele-based association variables. For the two-level genotype-based SNP markers (SNP2, SNP4, and SNP6), the absence or presence of the genotype was analyzed as the dichotomous variable as 0 (absence of the genotype) and 1 (presence of the genotype). For the three-level allele-based association SNP markers (SNP1, SNP3, and SNP5), the analysis was based on the number of copies of the allele (0, 1 and 2). Percentage of responders segregated on the basis of SNP marker variable were reported. |
| Time Frame | Day 1 of EMR200136_023 study |
| Safety Issue? | No |

Analysis Population Description

Evaluable population. Here, 'N' signifies number of participants who were evaluable for this outcome measure and 'n' signifies number of participants who were evaluable for the specified SNP categories.

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial pharmacogenetics (PGx) sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Measured Values

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| Number of Participants Analyzed | 135 | 149 |
| Percentage of Responders as Defined by Single Nucleotide Polymorphism (SNP) Markers<br>[units: percentage of participants] | | |

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| SNP1: 0 copy (n=63, 61) | 63.5 | 63.9 |
| SNP1: 1 copy (n=61, 73) | 65.6 | 60.3 |
| SNP1: 2 copies (n=11, 15) | 72.7 | 73.3 |
| SNP2: Present (n=106, 121) | 61.3 | 64.5 |
| SNP2: Absent (n=29, 28) | 79.3 | 57.1 |
| SNP3: 0 copy (n=62, 72) | 67.7 | 65.3 |
| SNP3: 1 copy (n=64, 62) | 60.9 | 56.5 |
| SNP3: 2 copies (n=9, 15) | 77.8 | 80.0 |
| SNP4: Present (n=73, 77) | 63.0 | 61.0 |
| SNP4: Absent (n=62, 72) | 67.7 | 65.3 |
| SNP5: 0 copy (n=58, 66) | 65.5 | 60.6 |
| SNP5: 1 copy (n=54, 67) | 64.8 | 67.2 |
| SNP5: 2 copies (n=23, 16) | 65.2 | 56.3 |
| SNP6: Present (n=18, 27) | 55.6 | 63.0 |
| SNP6: Absent (n=117, 122) | 66.7 | 63.1 |

2. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Number of Participants With Confirmed Expanded Disability Status Scale (EDSS) Progression as Defined by SNP2 Marker |
| Measure Description | EDSS assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death due to MS) was calculated. EDSS progression was defined as increase by at least 1 point if last value of EDSS was equal to 5.5, and by at least 0.5 points if last EDSS was more than 5.5. SNP2 is two-level genotype-based SNP marker. The absence or presence of the genotype was analyzed as the dichotomous variable as 0 (absence of the genotype) and 1 (presence of the genotype). Number of responders segregated on the basis of SNP2 marker variable were reported. |
| Time Frame | Day 1 of EMR200136_023 study |
| Safety Issue? | No |

Analysis Population Description

Evaluable population. Here, 'N' signifies number of participants who were evaluable for this outcome measure and 'n' signifies number of participants who were evaluable for the specified SNP categories.

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial pharmacogenetics (PGx) sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Measured Values

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| Number of Participants Analyzed | 135 | 151 |
| Number of Participants With Confirmed Expanded Disability Status Scale (EDSS) Progression as Defined by SNP2 Marker<br>[units: participants] | | |
| SNP2: Present (n=106, 123) | 16 | 16 |
| SNP2: Absent (n=29, 28) | 3 | 0 |

3. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change in Time Constant 1 Gadolinium (T1 Gd) Enhancing Lesion Volume as Defined by SNP3 and SNP4 Markers |
| Measure Description | Change in T1 Gd enhancing lesion volume was measured by using magnetic resonance imaging (MRI) scans. SNP4 is two-level genotype-based SNP marker. The absence or presence of the genotype was analyzed as the dichotomous variable as 0 (absence of the genotype) and 1 (presence of the genotype). SNP3 is a three-level allele-based association SNP markers. The analysis was based on the number of copies of the allele (0, 1 and 2). Change in T1 Gd enhancing lesion volume segregated on the basis of SNP3 and SNP4 marker variables were reported. |
| Time Frame | Baseline (Day 1 of 24735 [NCT00078338] study) and Day 1 of EMR200136_023 study |
| Safety Issue? | No |

Analysis Population Description

MRI evaluable population was defined to include all participants from the evaluable population who had at least one post-baseline MRI evaluation during study 24735. Here, 'N' signifies number of participants who were evaluable for this outcome measure and 'n' signifies number of participants who were evaluable for the specified SNP categories.

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial pharmacogenetics (PGx) sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Measured Values

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| Number of Participants Analyzed | 65 | 69 |
| Change in Time Constant 1 Gadolinium (T1 Gd) Enhancing Lesion Volume as Defined by SNP3 and SNP4 Markers<br>[units: cubic millimeter (mm^3)]<br>Mean (Standard Deviation) | | |
| SNP3: 0 copy (n=30, 42) | -524.23 (1481.03) | -203.71 (687.59) |
| SNP3: 1 copy (n=31, 22) | -106.97 (152.22) | -61.95 (232.25) |
| SNP3: 2 copies (n=4, 5) | -26.50 (53.00) | -22.80 (34.27) |
| SNP4: Present (n=35, 27) | -97.77 (146.18) | -54.70 (209.73) |
| SNP4: Absent (n=30, 42) | -524.23 (1481.03) | -203.71 (687.59) |

4. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change in Brain Volume as Defined by SNP2 Marker |
| Measure Description | Change in brain volume was measured as the brain parenchymal fraction using MRI scans. SNP2 is two-level genotype-based SNP marker. The absence or presence of the genotype was analyzed as the dichotomous variable as 0 (absence of the genotype) and 1 (presence of the genotype). Change in brain volume segregated on the basis of SNP2 marker variables were reported. |
| Time Frame | Baseline (Day 1 of 24735 [NCT00078338] study) and Day 1 of EMR200136_023 study |
| Safety Issue? | No |

Analysis Population Description

MRI evaluable population was defined to include all participants from the evaluable population who had at least one post-baseline MRI evaluation during study 24735. Here, 'N' signifies number of participants who were evaluable for this outcome measure and 'n' signifies number of participants who were evaluable for the specified SNP categories.

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial pharmacogenetics (PGx) sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Measured Values

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| Number of Participants Analyzed | 44 | 44 |
| Change in Brain Volume as Defined by SNP2 Marker<br>[units: cubic millimeter (mm^3)]<br>Mean (Standard Deviation) | | |
| SNP2: Present (n=33, 38) | -1.51 (1.60) | -1.10 (1.16) |
| SNP2: Absent (n=11, 6) | -0.57 (1.25) | -0.48 (0.41) |

5. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Mean Number of Time Constant 2 (T2) Active Lesions Per Subject Per Scan as Defined by SNP5 Marker |
| Measure Description | Mean number of T2 active lesions was measured by using MRI scans. SNP5 is a three-level allele-based association SNP markers. The analysis was based on the number of copies of the allele (0, 1 and 2). Mean number of T2 active lesions segregated on the basis of SNP5 marker variables were reported. |
| Time Frame | Day 1 of EMR200136_023 study |
| Safety Issue? | No |

Analysis Population Description

MRI evaluable population was defined to include all participants from the evaluable population who had at least one post-baseline MRI evaluation during study 24735. Here, 'N' signifies number of participants who were evaluable for this outcome measure and 'n' signifies number of participants who were evaluable for the specified SNP categories.

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial pharmacogenetics (PGx) sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Measured Values

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| Number of Participants Analyzed | 78 | 83 |
| Mean Number of Time Constant 2 (T2) Active Lesions Per Subject Per Scan as Defined by SNP5 Marker<br>[units: T2 lesions]<br>Mean (Standard Deviation) | | |
| SNP5: 0 copy (n=31, 42) | 0.72 (1.50) | 1.05 (1.32) |
| SNP5: 1 copy (n=36, 34) | 0.53 (1.41) | 0.55 (1.19) |
| SNP5: 2 copies (n=11, 7) | 0.30 (0.40) | 0.18 (0.37) |

## Reported Adverse Events

| | |
|---|---|
| Time Frame | [Not specified] |
| Additional Description | As it is a retrospective study, only serious adverse events which were considered by the investigator to be at least possibly related to the conduct of the trial, that is, the trial procedure (blood sampling), were collected. |

Reporting Groups

| | Description |
|---|---|
| Rebif® Cohort | Participants who had received Rebif® 44 microgram (mcg) three times a week for 96 weeks in study 24735 (NCT00078338) and not participated in the initial pharmacogenetics (PGx) sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

| | Description |
|---|---|
| Copaxone® Cohort | Participants who had received Copaxone® (Glatiramer Acetate) 20 milligram once daily for 96 weeks in study 24735 (NCT00078338) and not participated in the initial PGx sub-study were enrolled in this retrospective cohort study wherein single blood sampling was performed for pharmacogenetic markers analysis. |

Serious Adverse Events

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 0/158 (0%) | 0/166 (0%) |

Other Adverse Events

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

| | Rebif® Cohort | Copaxone® Cohort |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 0/0 | 0/0 |

## Limitations and Caveats

[Not specified]

## More Information

Certain Agreements:

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

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

PIs have to submit any publication for internal review and approval by EMD Serono before it can be publicly disclosed.

Results Point of Contact:

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