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Trial record **1 of 1** for: CFTY720D2309

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Efficacy and Safety of Fingolimod (FTY720) in Patients With Relapsing-remitting Multiple Sclerosis (FREEDOMS II)

This study has been completed.

Sponsor:
Novartis

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT00355134

First received: July 19, 2006
Last updated: August 2, 2012
Last verified: August 2012
History of Changes

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Results First Received: May 23, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Multiple Sclerosis
Interventions:	Drug: Fingolimod Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Patients were randomized to receive fingolimod 0.5 mg, 1.25 mg or placebo for up to 24 months. Upon entry into the Extension phase, patients treated with fingolimod 0.5 mg or 1.25 mg during the Core phase continued treatment at the same dose, those previously treated with placebo were re-randomized in to receive one of the two doses of fingolimod.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo (Core)	Participants received placebo capsules orally once a day for up to 24 months during the core phase. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.
Extension: Fingolimod 1.25 mg	Participants who had received placebo in the Core phase and then received 1.25 mg fingolimod orally once a day in the Extension phase. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Extension: Fingolimod 0.5 mg	Participants who had received placebo in the Core phase and then received 0.5 mg fingolimod orally once a day in the Extension phase.

Participant Flow for 2 periods

Period 1: Core Phase

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo (Core)	Extension: Fingolimod 1.25 mg	Extension: Fingolimod 0.5 mg
STARTED	370	358	355	0	0
COMPLETED	251	272	255	0	0
NOT COMPLETED	119	86	100	0	0
Withdrawal by Subject	35	24	35	0	0
Adverse Event	28	22	16	0	0
Lost to Follow-up	17	13	21	0	0
Abnormal laboratory value(s)	19	14	2	0	0
Unsatisfactory therapeutic effect	10	6	17	0	0
Administrative problems	5	3	5	0	0
Protocol Violation	3	2	2	0	0
Abnormal test procedure result(s)	1	2	1	0	0
Condition no longer requires study drug	1	0	1	0	0

Period 2: Extension Phase

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo (Core)	Extension: Fingolimod 1.25 mg	Extension: Fingolimod 0.5 mg
STARTED	203	217	0	105	107
COMPLETED	172	180	0	89	88

NOT COMPLETED	**31**	**37**	**0**	**16**	**19**
Withdrawal by Subject	**7**	**11**	**0**	**7**	**5**
Adverse Event	**13**	**9**	**0**	**3**	**5**
Lost to Follow-up	**2**	**6**	**0**	**2**	**4**
Abnormal laboratory value(s)	**4**	**2**	**0**	**2**	**2**
Administrative problems	**2**	**4**	**0**	**1**	**1**
Unsatisfactory therapeutic effect	**3**	**4**	**0**	**0**	**1**
Abnormal test procedure result(s)	**0**	**1**	**0**	**0**	**1**
Protocol Violation	**0**	**0**	**0**	**1**	**0**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.

Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo (Core)	Participants received placebo capsules orally once a day for up to 24 months during the core phase. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.
Extension: Fingolimod 1.25 mg	Participants who had received placebo in the Core phase and then received 1.25 mg fingolimod orally once a day in the Extension phase. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Extension: Fingolimod 0.5 mg	Participants who had received placebo in the Core phase and then received 0.5 mg fingolimod orally once a day in the Extension phase.
Total	Total of all reporting groups

Baseline Measures

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo (Core)	Extension: Fingolimod 1.25 mg	Extension: Fingolimod 0.5 mg	Total
Number of Participants [units: participants]	**370**	**358**	**355**	**105**	**107**	**1295**
Age [1] [units: years] Mean (Standard Deviation)	**40.9 (8.90)**	**40.6 (8.39)**	**40.1 (8.42)**	**NA [2]**	**NA [2]**	**40.5 (8.58)**
Age [3] [units: years] Mean (Standard Deviation)	**40.6 (8.71)**	**40.8 (7.96)**	**NA [4]**	**39.8 (8.32)**	**41.1 (8.11)**	**40.6 (8.28)**
Gender [1] [units: participants]						
Female	**281**	**275**	**288**	**0**	**0**	**844**

Male	**89**	**83**	**67**	**0**	**0**	**239**
Gender [3] [units: participants]						
Female	**148**	**160**	**0**	**88**	**85**	**481**
Male	**55**	**57**	**0**	**17**	**22**	**151**

[1] Demographic data for the Core phase participant population.
[2] Age demographic data presented for Core phase population only.
[3] Demographic data for the Extension phase population. The number of participants in each treatment group in the Extension phase was 203, 217, 0, 105 and 107; Total participants 632.
[4] Age demographic data presented for the Extension phase population only.

Outcome Measures

Hide All Outcome Measures

1. Primary: Aggregate Annualized Relapse Rate (ARR) Estimate up to Month 24 [Time Frame: 24 months]

Measure Type	Primary
Measure Title	Aggregate Annualized Relapse Rate (ARR) Estimate up to Month 24
Measure Description	ARR is the average number of relapses in a year calculated by negative binomial regression as the sum of confirmed relapses of all patients in the group divided by the sum of the number of days on study of all patients in the group and multiplied by 365.25. A relapse was defined as the appearance of a new neurological abnormality or worsening of previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding clinical demyelinating event. The abnormality must be present for at least 24 hours and occur in the absence of fever (<37.5C) or known infection. A relapse must be confirmed by the Independent Evaluating Physician (examining neurologist). ARR estimates were calculated from a negative binomial regression model adjusted for treatment, pooled center, number of relapses in the previous 2 years prior to enrollment, and Baseline expanded disability status scale (EDSS).

Time Frame	24 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set, including all patients who were randomized and took at least one dose of study drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Aggregate Annualized Relapse Rate (ARR) Estimate up to Month 24 [units: relapses per year] Number (95% Confidence Interval)	**0.203 (0.165 to 0.249)**	**0.208 (0.170 to 0.254)**	**0.403 (0.342 to 0.475)**

No statistical analysis provided for Aggregate Annualized Relapse Rate (ARR) Estimate up to Month 24

2. Secondary: Aggregate Annualized Relapse Rate (ARR) Estimate up to End of Study [Time Frame: From Baseline until end of study (up to approximately 54 months).]

Measure Type	Secondary
Measure Title	Aggregate Annualized Relapse Rate (ARR) Estimate up to End of Study
Measure Description	ARR is the average number of relapses in a year calculated by negative binomial regression as the sum of confirmed relapses of all patients in the group divided by the sum of the number of days on study of all patients in the group and multiplied by 365.25. A relapse was defined as the appearance of a new neurological abnormality or worsening of previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding clinical demyelinating event. The abnormality must be present for at least 24 hours and occur in the absence of fever (<37.5C) or known infection. A relapse must be confirmed by the Independent Evaluating Physician (examining neurologist). ARR estimates were calculated from a negative binomial regression model adjusted for treatment, pooled center, number of relapses in the previous 2 years prior to enrollment, and Baseline expanded disability status scale (EDSS).
Time Frame	From Baseline until end of study (up to approximately 54 months).
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension

	phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Aggregate Annualized Relapse Rate (ARR) Estimate up to End of Study [units: relapses per year] Number (95% Confidence Interval)	**0.180 (0.147 to 0.222)**	**0.192 (0.157 to 0.234)**	**0.363 (0.305 to 0.431)**

No statistical analysis provided for Aggregate Annualized Relapse Rate (ARR) Estimate up to End of Study

3. Secondary: Percent Change From Baseline in Brain Volume [Time Frame: Baseline, Month 24 and end of study (up to approximately 54 months)]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Brain Volume
Measure Description	Brain volume was measured using magnetic resonance imaging (MRI). Change from Baseline in brain volume is expressed as a percentage of the Baseline brain volume.

Time Frame	Baseline, Month 24 and end of study (up to approximately 54 months)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug. Patients were grouped according to the assigned treatment. "N" indicates the number of participants with data available for the specified time period.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Percent Change From Baseline in Brain Volume [units: percent change] Mean (Standard Deviation)			

Month 24 [N=247; 266; 249]	**-0.595 (1.3897)**	**-0.858 (1.2215)**	**-1.279 (1.5028)**
End of study [N=178; 187; 182]	**-1.130 (1.6380)**	**-1.266 (1.6941)**	**-1.694 (1.9567)**

No statistical analysis provided for Percent Change From Baseline in Brain Volume

4. Secondary: Number of New or Newly Enlarged T2 Lesions [Time Frame: From Baseline until Month 48]

Measure Type	Secondary
Measure Title	Number of New or Newly Enlarged T2 Lesions
Measure Description	Inflammatory disease activity was assessed by magnetic resonance imaging (MRI) measurement of the number of new or newly enlarged T2 lesions, by year.
Time Frame	From Baseline until Month 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug. Patients were grouped according to the assigned treatment. "N" indicates the number of participants with MRI data available for the specified time period.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension

	phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Number of New or Newly Enlarged T2 Lesions [units: lesions] Mean (Standard Deviation)			
Core Phase (Month 0 to 24) [N=245; 264; 251]	**1.6 (5.41)**	**2.3 (7.26)**	**8.9 (13.86)**
Month 24 to 36 [N=103; 111; 102]	**0.63 (2.856)**	**0.45 (1.360)**	**0.63 (1.455)**
Month 36 to 48 [N=24; 15; 15]	**0.13 (0.448)**	**0.07 (0.258)**	**2.53 (8.741)**

No statistical analysis provided for Number of New or Newly Enlarged T2 Lesions

5. Secondary: Number of Gadolinium-enhanced T1 Lesions [Time Frame: Month 24 and end of study (up to approximately 54 months)]

Measure Type	Secondary
Measure Title	Number of Gadolinium-enhanced T1 Lesions
Measure Description	Inflammatory disease activity was assessed by magnetic resonance imaging (MRI) measurement of the number of gadolinium-enhanced T1 lesions.
Time Frame	Month 24 and end of study (up to approximately 54 months)

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug. "N" indicates the number of participants with evaluable MRI data for the specified time point.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Number of Gadolinium-enhanced T1 Lesions [units: lesions] Mean (Standard Deviation)			
Core Phase (Month 24) [N=251; 269; 256]	**0.24 (2.395)**	**0.37 (1.841)**	**1.22 (2.967)**
End of Extension study [N=184; 194; 184]	**0.46 (2.381)**	**0.09 (0.308)**	**0.45 (3.618)**

No statistical analysis provided for Number of Gadolinium-enhanced T1 Lesions

6. Secondary: Change From Baseline in Lesion Volume at Month 24 (Core Phase) [Time Frame: Baseline and Month 24]

Measure Type	Secondary
Measure Title	Change From Baseline in Lesion Volume at Month 24 (Core Phase)
Measure Description	Change from Baseline in lesion volume was measured by MRI for T2 lesions and for T1 hypointense lesions.
Time Frame	Baseline and Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set for whom data were available. N=the number of patients with non-missing baseline and post-baseline values.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a

	day.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Change From Baseline in Lesion Volume at Month 24 (Core Phase) [units: mm^3] Mean (Standard Deviation)			
T2 lesions [N=248, 266, 251]	**-436.92 (1557.820)**	**-223.27 (1405.459)**	**541.83 (2830.868)**
T1 hypointense lesions [N=247, 266, 248]	**-99.13 (391.210)**	**-111.28 (530.961)**	**-37.68 (671.708)**

No statistical analysis provided for Change From Baseline in Lesion Volume at Month 24 (Core Phase)

7. Secondary: Percentage of Participants Free of 3-month Confirmed Disability Progression at Month 24 and End of Study [Time Frame: 24 months and end of study (up to approximately 54 months)]

Measure Type	Secondary
Measure Title	Percentage of Participants Free of 3-month Confirmed Disability Progression at Month 24 and End of Study
Measure Description	Disability progression was defined using the following criteria: One point increase from baseline in patients with Baseline Expanded Disability Status Scale (EDSS) score from 0 to 5.0; or half a point increase from Baseline in patients with Baseline EDSS score of 5.5 or above. A 3-month confirmed disability progression was defined as a 3-month sustained increase from Baseline in EDSS score. The EDSS quantifies disability in multiple sclerosis in 8 functional systems; the score ranges from 0 (normal) to 10 (death due to MS). Progression curves were generated by the Kaplan–Meier method.
Time Frame	24 months and end of study (up to approximately 54 months)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo**
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Percentage of Participants Free of 3-month Confirmed Disability Progression at Month 24 and End of Study [units: percentage of participants] Number (95% Confidence Interval)			
At month 24	**78.3 (73.74 to 82.87)**	**74.7 (69.86 to 79.52)**	**71.0 (65.94 to 76.13)**

At end of study	**66.64 (59.81 to 73.47)**	**58.89 (48.98 to 68.80)**	**63.51 (57.15 to 69.87)**

No statistical analysis provided for Percentage of Participants Free of 3-month Confirmed Disability Progression at Month 24 and End of Study

8. Secondary: Percentage of Participants Free of 6-month Confirmed Disability Progression at Month 24 and End of Study [Time Frame: 24 months and end of study (up to approximately 54 months)]

Measure Type	Secondary
Measure Title	Percentage of Participants Free of 6-month Confirmed Disability Progression at Month 24 and End of Study
Measure Description	Disability progression was defined using the following criteria: One point increase from baseline in patients with Baseline Expanded Disability Status Scale (EDSS) score from 0 to 5.0; or half a point increase from Baseline in patients with Baseline EDSS score of 5.5 or above. A 6-month confirmed disability progression was defined as a 6-month sustained increase from Baseline in EDSS score. The EDSS quantifies disability in multiple sclerosis in 8 functional systems; the score ranges from 0 (normal) to 10 (death due to MS). Progression curves were generated by the Kaplan-Meier method.
Time Frame	24 months and end of study (up to approximately 54 months)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug.

Reporting Groups

	Description

Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Percentage of Participants Free of 6-month Confirmed Disability Progression at Month 24 and End of Study [units: percentage of participants] Number (95% Confidence Interval)			
At Month 24	**86.9 (83.16 to 90.61)**	**86.2 (82.34 to 89.97)**	**82.2 (77.90 to 86.44)**
At end of study	**79.92 (74.43 to 85.41)**	**74.89 (68.36 to 81.43)**	**75.03 (69.59 to 80.47)**

No statistical analysis provided for Percentage of Participants Free of 6-month Confirmed Disability Progression at Month 24 and End of Study

9. Secondary: Percentage of Participants Relapse-free up to Month 24 [Time Frame: 24 months]

Measure Type	Secondary
Measure Title	Percentage of Participants Relapse-free up to Month 24
Measure Description	Estimates of the percentage of participants relapse-free at 24 months were generated from Kaplan-Meier curves of the time to first relapse. A relapse was defined as the appearance of a new neurological abnormality or worsening of previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding clinical demyelinating event. The abnormality must be present for at least 24 hours and occur in the absence of fever (<37.5C) or infection. A relapse was confirmed by an Independent Evaluating Physician.
Time Frame	24 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Percentage of Participants Relapse-free up to Month 24 [units: percentage of participants] Number (95% Confidence Interval)	**73.2 (68.38 to 78.01)**	**71.5 (66.55 to 76.44)**	**52.7 (47.20 to 58.24)**

No statistical analysis provided for Percentage of Participants Relapse-free up to Month 24

10. Secondary: Percentage of Participants Relapse-free up to End of Study [Time Frame: From Baseline until the end of study (up to approximately 54 months)]

Measure Type	Secondary
Measure Title	Percentage of Participants Relapse-free up to End of Study
Measure Description	Estimates of the percentage of participants relapse-free at end of study were generated from Kaplan-Meier curves of the time to first relapse. A relapse was defined as the appearance of a new neurological abnormality or worsening of previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding clinical demyelinating event. The abnormality must be present for at least 24 hours and occur in the absence of fever (<37.5C) or infection. A relapse was confirmed by an Independent Evaluating Physician.
Time Frame	From Baseline until the end of study (up to approximately 54 months)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo
Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Percentage of Participants Relapse-free up to End of Study [units: percentage of participants] Number (95% Confidence Interval)	**63.88 (56.19 to 71.57)**	**66.57 (60.86 to 72.28)**	**49.12 (43.35 to 54.89)**

No statistical analysis provided for Percentage of Participants Relapse-free up to End of Study

11. Secondary: Change From Baseline in Multiple Sclerosis Functional Composite (MSFC) Z-score [Time Frame: Baseline, Month 24 and end of study (up to approximately 54 months)]

Measure Type	Secondary
Measure Title	Change From Baseline in Multiple Sclerosis Functional Composite (MSFC) Z-score

Measure Description	The Multiple Sclerosis Functional Composite (MSFC) is a multidimensional clinical outcome measure that includes quantitative tests of leg function/ambulation (Timed 25-Foot Walk), arm function (9-Hole Peg Test), and cognitive function (Paced Auditory Serial Addition Test). The overall MSFC z-score as an average of the three standardized scores derived using baseline data pooled over each treatment arm as reference population. Higher scores reflect better neurological function and a positive change from Baseline indicates improvement.
Time Frame	Baseline, Month 24 and end of study (up to approximately 54 months)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Core intent-to-treat (ITT) population: All patients who were randomized in the Core phase and received at least one dose of Core phase drug. "N" indicates the number of participants with non-missing data at each time point.

Reporting Groups

	Description
Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 1.25 mg fingolimod orally. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase. In the Extension phase participants continued to receive 0.5 mg fingolimod orally once a day.
Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. In the Extension phase participants received either 1.25 or 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo**

Number of Participants Analyzed [units: participants]	**370**	**358**	**355**
Change From Baseline in Multiple Sclerosis Functional Composite (MSFC) Z-score [units: units on a scale] Mean (Standard Deviation)			
Month 24 [N=250; 271; 258]	**-0.08 (0.916)**	**0.00 (0.600)**	**-0.07 (0.540)**
End of Study [N=174; 187; 184]	**0.011 (0.3499)**	**-0.091 (0.8770)**	**0.019 (0.6304)**

No statistical analysis provided for Change From Baseline in Multiple Sclerosis Functional Composite (MSFC) Z-score

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Duration of treatment was up to 24 months during the Core phase, and dependent on the length of patient participation during the Extension phase (up to approximately 54 months overall duration of treatment).
Additional Description	No text entered.

Reporting Groups

	Description
Core: Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Core: Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase.
Core: Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.

Extension: Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day in the Extension phase. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Extension: Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day in the Extension phase.

Serious Adverse Events

	Core: Fingolimod 1.25 mg	Core: Fingolimod 0.5 mg	Core: Placebo	Extension: Fingolimod 1.25 mg	Extension: Fingolimod 0.5 mg
Total, serious adverse events					
# participants affected / at risk	**53/370 (14.32%)**	**53/358 (14.80%)**	**45/355 (12.68%)**	**27/308 (8.77%)**	**21/324 (6.48%)**
Blood and lymphatic system disorders					
Idiopathic thrombocytopenic purpura † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Leukopenia † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Lymphopenia † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**1/324 (0.31%)**
Cardiac disorders					
Acute coronary syndrome † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Acute myocardial infarction † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Angina pectoris † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**2/355 (0.56%)**	**1/308 (0.32%)**	**0/324 (0.00%)**

Atrial fibrillation † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Atrioventricular block † 1					
# participants affected / at risk	**2/370 (0.54%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Atrioventricular block first degree † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Atrioventricular block second degree † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Bradycardia † 1					
# participants affected / at risk	**6/370 (1.62%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**2/308 (0.65%)**	**0/324 (0.00%)**
Cardiac flutter † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Coronary artery disease † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Mitral valve incompetence † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Palpitations † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Pericarditis † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Tricuspid valve incompetence † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Ventricular tachycardia † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Endocrine disorders					

Diabetes insipidus † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Hyperthyroidism † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Eye disorders					
Macular oedema † 1					
# participants affected / at risk	**2/370 (0.54%)**	**1/358 (0.28%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Retinal detachment † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Gastrointestinal disorders					
Abdominal hernia † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Abdominal mass † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Abdominal pain † 1					
# participants affected / at risk	**1/370 (0.27%)**	**2/358 (0.56%)**	**2/355 (0.56%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Abdominal pain lower † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Caecitis † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Constipation † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Diarrhoea † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Gastric disorder † 1					

# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Hiatus hernia † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Intestinal obstruction † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Large intestine perforation † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Vomiting † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
General disorders					
Asthenia † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Chest discomfort † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Chest pain † 1					
# participants affected / at risk	1/370 (0.27%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	1/324 (0.31%)
Fatigue † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Non-cardiac chest pain † 1					
# participants affected / at risk	0/370 (0.00%)	2/358 (0.56%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Pelvic mass † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Pyrexia † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Hepatobiliary disorders					

Bile duct stone † [1]					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Cholecystitis † [1]					
# participants affected / at risk	**2/370 (0.54%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Cholelithiasis † [1]					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**2/355 (0.56%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Jaundice † [1]					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Immune system disorders					
Drug hypersensitivity † [1]					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Infections and infestations					
Acute sinusitis † [1]					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Appendicitis † [1]					
# participants affected / at risk	**0/370 (0.00%)**	**2/358 (0.56%)**	**1/355 (0.28%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Bartholin's abscess † [1]					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Bronchitis † [1]					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Cellulitis † [1]					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Diverticulitis † [1]					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Encephalitis herpes † [1]					

# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Gastritis viral † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)
Gastroenteritis † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)
Gastroenteritis viral † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Hepatitis C † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Herpes zoster † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Herpes zoster disseminated † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Kidney infection † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Labyrinthitis † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Lower respiratory tract infection fungal † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Lyme disease † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Mastoiditis † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Otitis media † 1					

# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Pneumonia † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	1/324 (0.31%)
Post procedural infection † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)
Pyelonephritis † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Sinusitis † 1					
# participants affected / at risk	0/370 (0.00%)	2/358 (0.56%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Staphylococcal abscess † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Staphylococcal infection † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Urinary tract infection † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	1/355 (0.28%)	1/308 (0.32%)	0/324 (0.00%)
Vulvitis † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Injury, poisoning and procedural complications					
Ankle fracture † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Drug exposure during pregnancy † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Injury † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)

Joint dislocation † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Laceration † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Lower limb fracture † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**1/324 (0.31%)**
Overdose † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Post procedural haemorrhage † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Toxicity to various agents † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Investigations					
Alanine aminotransferase increased † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Hepatic enzyme increased † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Metabolism and nutrition disorders					
Dehydration † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Hypokalaemia † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Hyponatraemia † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Hypophosphataemia † 1					

# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Metabolic acidosis † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Musculoskeletal and connective tissue disorders					
Arthralgia † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Back pain † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Intervertebral disc degeneration † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Intervertebral disc protrusion † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Mobility decreased † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Morphoea † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Musculoskeletal chest pain † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	1/324 (0.31%)
Myalgia † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Neck pain † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)
Spinal column stenosis † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)

Spinal osteoarthritis † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Astrocytoma † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Basal cell carcinoma † 1					
# participants affected / at risk	**6/370 (1.62%)**	**9/358 (2.51%)**	**2/355 (0.56%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Breast cancer † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**1/324 (0.31%)**
Colon cancer † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Dysplastic naevus † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Endometrial cancer † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Ependymoma † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Hair follicle tumour benign † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Malignant melanoma in situ † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Melanocytic naevus † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**1/324 (0.31%)**
Parathyroid tumour benign † 1					

# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	1/324 (0.31%)
Sarcoma of skin † [1]					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Squamous cell carcinoma † [1]					
# participants affected / at risk	3/370 (0.81%)	1/358 (0.28%)	2/355 (0.56%)	1/308 (0.32%)	1/324 (0.31%)
Squamous cell carcinoma of skin † [1]					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)
T-cell lymphoma † [1]					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Thyroid adenoma † [1]					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)
Thyroid cancer † [1]					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Uterine leiomyoma † [1]					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	2/355 (0.56%)	1/308 (0.32%)	0/324 (0.00%)
Nervous system disorders					
Akathisia † [1]					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Convulsion † [1]					
# participants affected / at risk	0/370 (0.00%)	3/358 (0.84%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Encephalitis † [1]					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Encephalopathy † [1]					
# participants affected / at risk	2/370 (0.54%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Grand mal convulsion † [1]					

# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Haemorrhagic stroke † [1]					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Headache † [1]					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	1/308 (0.32%)	0/324 (0.00%)
Intracranial aneurysm † [1]					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	1/308 (0.32%)	0/324 (0.00%)
Migraine † [1]					
# participants affected / at risk	1/370 (0.27%)	1/358 (0.28%)	2/355 (0.56%)	1/308 (0.32%)	0/324 (0.00%)
Multiple sclerosis relapse † [1]					
# participants affected / at risk	2/370 (0.54%)	1/358 (0.28%)	3/355 (0.85%)	2/308 (0.65%)	5/324 (1.54%)
Optic neuritis † [1]					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Sciatica † [1]					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Simple partial seizures † [1]					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Status epilepticus † [1]					
# participants affected / at risk	1/370 (0.27%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Syncope † [1]					
# participants affected / at risk	2/370 (0.54%)	2/358 (0.56%)	1/355 (0.28%)	1/308 (0.32%)	1/324 (0.31%)
Transient ischaemic attack † [1]					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Pregnancy, puerperium and perinatal conditions					

Abortion † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Abortion spontaneous † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Ectopic pregnancy † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Psychiatric disorders					
Acute psychosis † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Aggression † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Anxiety † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Confusional state † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Depression † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**2/355 (0.56%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Drug dependence † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Frustration † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Hallucination † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Major depression † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**3/355 (0.85%)**	**0/308 (0.00%)**	**0/324 (0.00%)**

Mania † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Mental disorder † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**2/355 (0.56%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Mental status changes † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Paranoia † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Suicidal behaviour † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Suicidal ideation † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Renal and urinary disorders					
Chromaturia † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Nephrolithiasis † 1					
# participants affected / at risk	**0/370 (0.00%)**	**3/358 (0.84%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Renal colic † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Reproductive system and breast disorders					
Adenomyosis † 1					
# participants affected / at risk	**0/370 (0.00%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Cervical cyst † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Cervical dysplasia † 1					

# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	1/324 (0.31%)
Cystocele † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Haemorrhagic ovarian cyst † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Menorrhagia † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	1/308 (0.32%)	0/324 (0.00%)
Ovarian cyst † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Pelvic pain † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	1/355 (0.28%)	0/308 (0.00%)	0/324 (0.00%)
Rectocele † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Uterine prolapse † 1					
# participants affected / at risk	0/370 (0.00%)	0/358 (0.00%)	2/355 (0.56%)	0/308 (0.00%)	0/324 (0.00%)
Uterovaginal prolapse † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Vaginal haemorrhage † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Respiratory, thoracic and mediastinal disorders					
Asthma † 1					
# participants affected / at risk	1/370 (0.27%)	0/358 (0.00%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)
Bronchospasm † 1					
# participants affected / at risk	0/370 (0.00%)	1/358 (0.28%)	0/355 (0.00%)	0/308 (0.00%)	0/324 (0.00%)

Dyspnoea † 1					
# participants affected / at risk	**1/370 (0.27%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Pulmonary embolism † 1					
# participants affected / at risk	**1/370 (0.27%)**	**1/358 (0.28%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Wheezing † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Skin and subcutaneous tissue disorders					
Urticaria † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Surgical and medical procedures					
Abortion induced † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**1/308 (0.32%)**	**0/324 (0.00%)**
Vascular disorders					
Aortic dissection † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**1/355 (0.28%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Embolism † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Haemorrhage † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Hypertension † 1					
# participants affected / at risk	**1/370 (0.27%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**0/324 (0.00%)**
Orthostatic hypotension † 1					
# participants affected / at risk	**0/370 (0.00%)**	**0/358 (0.00%)**	**0/355 (0.00%)**	**0/308 (0.00%)**	**1/324 (0.31%)**

† Events were collected by systematic assessment

1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	Duration of treatment was up to 24 months during the Core phase, and dependent on the length of patient participation during the Extension phase (up to approximately 54 months overall duration of treatment).
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Core: Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day for up to 24 months during the core phase. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Core: Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day for up to 24 months during the core phase.
Core: Placebo	Participants received placebo capsules orally once a day for up to 24 months during the core phase. Upon implementation of a protocol amendment, all patients taking placebo were switched to 0.5 mg fingolimod orally once a day.
Extension: Fingolimod 1.25 mg	Participants received 1.25 mg fingolimod orally once a day in the Extension phase. Upon implementation of a protocol amendment, all patients taking 1.25 mg fingolimod were switched to 0.5 mg fingolimod orally once a day.
Extension: Fingolimod 0.5 mg	Participants received 0.5 mg fingolimod orally once a day in the Extension phase.

Other Adverse Events

	Core: Fingolimod 1.25	**Core: Fingolimod 0.5**	**Core: Placebo**	**Extension: Fingolimod 1.25**	**Extension: Fingolimod 0.5**

	mg	mg		mg	mg
Total, other (not including serious) adverse events					
# participants affected / at risk	**335/370 (90.54%)**	**320/358 (89.39%)**	**305/355 (85.92%)**	**216/308 (70.13%)**	**223/324 (68.83%)**
Blood and lymphatic system disorders					
Lymphopenia † 1					
# participants affected / at risk	**36/370 (9.73%)**	**26/358 (7.26%)**	**0/355 (0.00%)**	**25/308 (8.12%)**	**19/324 (5.86%)**
Eye disorders					
Vision blurred † 1					
# participants affected / at risk	**8/370 (2.16%)**	**18/358 (5.03%)**	**12/355 (3.38%)**	**4/308 (1.30%)**	**8/324 (2.47%)**
Gastrointestinal disorders					
Abdominal pain upper † 1					
# participants affected / at risk	**9/370 (2.43%)**	**18/358 (5.03%)**	**7/355 (1.97%)**	**3/308 (0.97%)**	**2/324 (0.62%)**
Diarrhoea † 1					
# participants affected / at risk	**52/370 (14.05%)**	**48/358 (13.41%)**	**43/355 (12.11%)**	**13/308 (4.22%)**	**16/324 (4.94%)**
Dyspepsia † 1					
# participants affected / at risk	**18/370 (4.86%)**	**12/358 (3.35%)**	**18/355 (5.07%)**	**4/308 (1.30%)**	**3/324 (0.93%)**
Nausea † 1					
# participants affected / at risk	**57/370 (15.41%)**	**63/358 (17.60%)**	**54/355 (15.21%)**	**13/308 (4.22%)**	**14/324 (4.32%)**
Vomiting † 1					
# participants affected / at risk	**29/370 (7.84%)**	**21/358 (5.87%)**	**27/355 (7.61%)**	**6/308 (1.95%)**	**8/324 (2.47%)**
General disorders					

Fatigue † 1					
# participants affected / at risk	**29/370 (7.84%)**	**22/358 (6.15%)**	**25/355 (7.04%)**	**12/308 (3.90%)**	**3/324 (0.93%)**
Pain † 1					
# participants affected / at risk	**21/370 (5.68%)**	**10/358 (2.79%)**	**15/355 (4.23%)**	**8/308 (2.60%)**	**7/324 (2.16%)**
Pyrexia † 1					
# participants affected / at risk	**16/370 (4.32%)**	**14/358 (3.91%)**	**20/355 (5.63%)**	**2/308 (0.65%)**	**5/324 (1.54%)**
Infections and infestations					
Bronchitis † 1					
# participants affected / at risk	**34/370 (9.19%)**	**29/358 (8.10%)**	**20/355 (5.63%)**	**18/308 (5.84%)**	**19/324 (5.86%)**
Influenza † 1					
# participants affected / at risk	**26/370 (7.03%)**	**34/358 (9.50%)**	**24/355 (6.76%)**	**11/308 (3.57%)**	**11/324 (3.40%)**
Nasopharyngitis † 1					
# participants affected / at risk	**88/370 (23.78%)**	**84/358 (23.46%)**	**85/355 (23.94%)**	**50/308 (16.23%)**	**52/324 (16.05%)**
Sinusitis † 1					
# participants affected / at risk	**45/370 (12.16%)**	**55/358 (15.36%)**	**45/355 (12.68%)**	**31/308 (10.06%)**	**27/324 (8.33%)**
Upper respiratory tract infection † 1					
# participants affected / at risk	**92/370 (24.86%)**	**87/358 (24.30%)**	**86/355 (24.23%)**	**49/308 (15.91%)**	**40/324 (12.35%)**
Urinary tract infection † 1					
# participants affected / at risk	**45/370 (12.16%)**	**47/358 (13.13%)**	**54/355 (15.21%)**	**23/308 (7.47%)**	**24/324 (7.41%)**
Injury, poisoning and procedural complications					
Fall † 1					

# participants affected / at risk	16/370 (4.32%)	22/358 (6.15%)	16/355 (4.51%)	14/308 (4.55%)	11/324 (3.40%)
Investigations					
Alanine aminotransferase increased † [1]					
# participants affected / at risk	35/370 (9.46%)	29/358 (8.10%)	6/355 (1.69%)	4/308 (1.30%)	13/324 (4.01%)
Gamma-glutamyltransferase increased † [1]					
# participants affected / at risk	21/370 (5.68%)	23/358 (6.42%)	2/355 (0.56%)	2/308 (0.65%)	8/324 (2.47%)
Lymphocyte count decreased † [1]					
# participants affected / at risk	20/370 (5.41%)	13/358 (3.63%)	0/355 (0.00%)	16/308 (5.19%)	20/324 (6.17%)
Musculoskeletal and connective tissue disorders					
Arthralgia † [1]					
# participants affected / at risk	36/370 (9.73%)	30/358 (8.38%)	38/355 (10.70%)	15/308 (4.87%)	10/324 (3.09%)
Back pain † [1]					
# participants affected / at risk	34/370 (9.19%)	29/358 (8.10%)	39/355 (10.99%)	20/308 (6.49%)	17/324 (5.25%)
Neck pain † [1]					
# participants affected / at risk	21/370 (5.68%)	14/358 (3.91%)	16/355 (4.51%)	5/308 (1.62%)	7/324 (2.16%)
Pain in extremity † [1]					
# participants affected / at risk	36/370 (9.73%)	44/358 (12.29%)	27/355 (7.61%)	20/308 (6.49%)	8/324 (2.47%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Melanocytic naevus † [1]					
# participants affected / at risk	33/370 (8.92%)	38/358 (10.61%)	44/355 (12.39%)	18/308 (5.84%)	21/324 (6.48%)

Nervous system disorders					
Dizziness † [1]					
# participants affected / at risk	**53/370 (14.32%)**	**38/358 (10.61%)**	**43/355 (12.11%)**	**10/308 (3.25%)**	**11/324 (3.40%)**
Headache † [1]					
# participants affected / at risk	**81/370 (21.89%)**	**83/358 (23.18%)**	**76/355 (21.41%)**	**25/308 (8.12%)**	**29/324 (8.95%)**
Migraine † [1]					
# participants affected / at risk	**15/370 (4.05%)**	**24/358 (6.70%)**	**19/355 (5.35%)**	**2/308 (0.65%)**	**8/324 (2.47%)**
Paraesthesia † [1]					
# participants affected / at risk	**14/370 (3.78%)**	**19/358 (5.31%)**	**18/355 (5.07%)**	**5/308 (1.62%)**	**5/324 (1.54%)**
Psychiatric disorders					
Anxiety † [1]					
# participants affected / at risk	**18/370 (4.86%)**	**18/358 (5.03%)**	**17/355 (4.79%)**	**5/308 (1.62%)**	**5/324 (1.54%)**
Depression † [1]					
# participants affected / at risk	**34/370 (9.19%)**	**29/358 (8.10%)**	**32/355 (9.01%)**	**11/308 (3.57%)**	**13/324 (4.01%)**
Insomnia † [1]					
# participants affected / at risk	**24/370 (6.49%)**	**31/358 (8.66%)**	**24/355 (6.76%)**	**2/308 (0.65%)**	**6/324 (1.85%)**
Respiratory, thoracic and mediastinal disorders					
Cough † [1]					
# participants affected / at risk	**51/370 (13.78%)**	**52/358 (14.53%)**	**53/355 (14.93%)**	**23/308 (7.47%)**	**24/324 (7.41%)**
Dyspnoea † [1]					
# participants affected / at risk	**46/370 (12.43%)**	**34/358 (9.50%)**	**33/355 (9.30%)**	**6/308 (1.95%)**	**6/324 (1.85%)**
Nasal congestion † [1]					

# participants affected / at risk	**23/370 (6.22%)**	**17/358 (4.75%)**	**21/355 (5.92%)**	**7/308 (2.27%)**	**6/324 (1.85%)**
Oropharyngeal pain † 1					
# participants affected / at risk	**25/370 (6.76%)**	**29/358 (8.10%)**	**32/355 (9.01%)**	**12/308 (3.90%)**	**9/324 (2.78%)**
Skin and subcutaneous tissue disorders					
Rash † 1					
# participants affected / at risk	**21/370 (5.68%)**	**22/358 (6.15%)**	**24/355 (6.76%)**	**14/308 (4.55%)**	**12/324 (3.70%)**
Vascular disorders					
Hypertension † 1					
# participants affected / at risk	**46/370 (12.43%)**	**32/358 (8.94%)**	**11/355 (3.10%)**	**11/308 (3.57%)**	**6/324 (1.85%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ 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**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ 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 **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300

No publications provided by Novartis

Publications automatically indexed to this study:

Chinea Martinez AR, Correale J, Coyle PK, Meng X, Tenenbaum N. Efficacy and safety of fingolimod in Hispanic patients with multiple sclerosis: pooled clinical trial analyses. Adv Ther. 2014 Oct;31(10):1072-81. doi: 10.1007/s12325-014-0154-4. Epub 2014 Sep 23.

Winges KM, Werner JS, Harvey DJ, Cello KE, Durbin MK, Balcer LJ, Calabresi PA, Keltner JL. Baseline retinal nerve fiber layer thickness and macular volume quantified by OCT in the North American phase 3 fingolimod trial for relapsing-remitting multiple sclerosis. J Neuroophthalmol. 2013 Dec;33(4):322-9. doi: 10.1097/WNO.0b013e31829c51f7.

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