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Trial record **1 of 1** for: CFTY720D2301E1

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

This study has been completed.

Sponsor:
Novartis

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT00662649

First received: April 17, 2008
Last updated: June 9, 2012
Last verified: June 2012
History of Changes

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Results First Received: June 9, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator); Primary Purpose: Treatment
Condition:	Multiple Sclerosis
Interventions:	Drug: Fingolimod 0.5 mg Drug: Fingolimod 1.25 mg

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
Of the 1272 patients randomly assigned to treatment in the Core study (ClinicalTrials.gov ID NCT00289978), 1033 completed the 24-month double-blind treatment phase and were eligible to enter the Extension study. A total of 920 of the 1033 patients entered the Extension study and received treatment.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo	Patients randomized to placebo in the Core study who were subsequently re-randomized to fingolimod(either 1.25 or 0.5 mg/day) in the Extension study.
Placebo-fingolimod 1.25 mg	Patients randomized to placebo in the core study were re randomized to fingolimod 1.25 mg/day in this extension study.
Placebo-fingolimod 0.5	Patients randomized to placebo in the core study were re randomized to fingolimod 0.5 mg/day in this extension study.

Participant Flow for 2 periods

Period 1: Core Study (24 Months)

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo	Placebo-fingolimod 1.25 mg	Placebo-fingolimod 0.5
STARTED	429	425	418	0 [1]	0 [1]
Intent to Treat (ITT)	429	425	418	0	0
COMPLETED	332	369	332	0	0
NOT COMPLETED	97	56	86	0	0
Withdrawal by Subject	31	17	28	0	0
Adverse Event	22	13	18	0	0
Unsatisfactory therapeutic effect	13	6	25	0	0
Abnormal laboratory value(s)	20	9	1	0	0
Lost to Follow-up	3	5	7	0	0
Protocol Violation	5	5	4	0	0
Abnormal test procedure result(s)	2	1	1	0	0
Death	1	0	2	0	0

[1] This reporting group is used only in extension study.

Period 2: Extension Study (Month 24 to 60)

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo	Placebo-fingolimod 1.25 mg	Placebo-fingolimod 0.5

STARTED	**289**	**331**	**0** [1]	**145**	**155**
Extension Intent to Treat Population	**287**	**330**	**0**	**145**	**154**
From Beginning of Core at Month 24	**289**	**331**	**0**	**145**	**155**
From Beginning of Core at Month 30	**276**	**324**	**0**	**136**	**152**
From Beginning of Core at Month 36	**270**	**311**	**0**	**130**	**145**
From Beginning of Core at Month 42	**254**	**301**	**0**	**120**	**136**
From Beginning of Core at Month 48	**125**	**152**	**0**	**58**	**67**
From Beginning of Core at Month 54	**31**	**32**	**0**	**11**	**13**
COMPLETED	**245** [2]	**290**	**0**	**112**	**126**
NOT COMPLETED	**44**	**41**	**0**	**33**	**29**
Abnormal laboratory value(s)	**10**	**5**	**0**	**8**	**3**
Abnormal test procedure result(s)	**3**	**1**	**0**	**1**	**3**
Administrative problems	**0**	**0**	**0**	**1**	**0**
Adverse Event	**6**	**9**	**0**	**6**	**10**
Lost to Follow-up	**2**	**0**	**0**	**1**	**1**

Protocol Violation	**1**	**1**	**0**	**0**	**0**
Subject withdrew consent	**19**	**23**	**0**	**15**	**9**
Subject no longer requires study drug	**0**	**1**	**0**	**0**	**0**
Unsatisfactory therapeutic effect	**3**	**1**	**0**	**1**	**3**

[1] This reporting group is used only for core study
[2] "completed" refers to patients that completed extension study in different time points.

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	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod 1.25 mg	Patients randomized to placebo in the core study were re randomized to fingolimod 1.25 mg/day in this extension study.
Placebo-fingolimod 0.5 mg	Patients randomized to placebo in the core study were re randomized to fingolimod 0.5 mg/day in this

	extension study.
Total	Total of all reporting groups

Baseline Measures

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo-fingolimod 1.25 mg	Placebo-fingolimod 0.5 mg	Total
Number of Participants [units: participants]	**289**	**331**	**145**	**155**	**920**
Age [1] [units: years] Mean (Standard Deviation)	**37.2 (8.87)**	**36.5 (8.60)**	**36.6 (9.21)**	**38.1 (8.26)**	**37.0 (8.73)**
Gender [units: participants]					
Female	**204**	**234**	**107**	**106**	**651**
Male	**85**	**97**	**38**	**49**	**269**

[1] All demographic measurements are based on extension randomized/safety population.

Outcome Measures

Hide All Outcome Measures

1. Primary: Annualized Aggregate Relapse Rate (ARR) During Months 0 to End of Study(Core [CFTY720D2301/NCT00289978] and Extension Study) [Time Frame: Months 0 to end of study (maximum up to 60 months)]

Measure Type	Primary
Measure Title	Annualized Aggregate Relapse Rate (ARR) During Months 0 to End of Study(Core [CFTY720D2301/NCT00289978] and Extension Study)

Measure Description	ARR is defined as the number of confirmed relapses in a year. A relapse is defined as the appearance of a new or worsening of a previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding relapse. The abnormality must be present for at least 24 hours and occur in the absence of fever or infection. The annualized ARR for each treatment group was the mean of the annualized ARRs for all patients in the group, calculated as the total number of confirmed relapses divided by the total number of days on study multiplied by 365.25.
Time Frame	Months 0 to end of study (maximum up to 60 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 study and received at least 1 dose of Core study drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod	Patients randomized to placebo in the Core study who were subsequently re-randomized to FTY720 (either 1.25 or 0.5 mg/day) in the Extension study.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo-fingolimod**
Number of Participants Analyzed [units: participants]	**429**	**425**	**418**
Annualized Aggregate Relapse Rate (ARR) During Months 0 to End of Study(Core			

[CFTY720D2301/NCT00289978] and Extension Study) **[units: Relapses per year]** **Number (95% Confidence Interval)**	**0.164** **(0.138 to 0.195)**	**0.185** **(0.158 to 0.217)**	**0.357** **(0.310 to 0.411)**

No statistical analysis provided for Annualized Aggregate Relapse Rate (ARR) During Months 0 to End of Study(Core [CFTY720D2301/NCT00289978] and Extension Study)

2. Primary: Time to First Confirmed Relapse up to End of Study: Kaplan-Meier Estimate of Percentage of Patients Relapse-free [Time Frame: Core baseline to end of study (maximum up to 60 months)]

Measure Type	Primary
Measure Title	Time to First Confirmed Relapse up to End of Study: Kaplan-Meier Estimate of Percentage of Patients Relapse-free
Measure Description	A relapse was confirmed when it was accompanied by an increase of at least half a step (0.5) on the Expanded Disability Status Scale (EDSS) or an increase of 1 point on two different Functional Systems (FS) of the EDSS or 2 points on one of the FS (excluding Bowel/Bladder or Cerebral FS). Kaplan-Meier estimates of the percentage of relapse-free patients at end of study and and 95% confidence intervals (CIs) were presented for the treatment groups.
Time Frame	Core baseline to end of study (maximum up to 60 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 study and received at least 1 dose of Core study drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.

Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod	Patients randomized to placebo in the Core study who were subsequently re-randomized to FTY720 (either 1.25 or 0.5 mg/day) in the Extension study.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo-fingolimod
Number of Participants Analyzed [units: participants]	**429**	**425**	**418**
Time to First Confirmed Relapse up to End of Study: Kaplan-Meier Estimate of Percentage of Patients Relapse-free [units: Percentage of patients] Number (95% Confidence Interval)	**59.85 (53.90 to 65.80)**	**59.29 (54.17 to 64.41)**	**37.18 (32.15 to 42.22)**

No statistical analysis provided for Time to First Confirmed Relapse up to End of Study: Kaplan-Meier Estimate of Percentage of Patients Relapse-free

3. Primary: Annualized Aggregate Relapse Rate (ARR) During Months 0-24 (Core Study) and Months 24-48 (Extension Study) [Time Frame: Months 0-24 (core study) and Months 24-48 (extension study)]

Measure Type	Primary
Measure Title	Annualized Aggregate Relapse Rate (ARR) During Months 0-24 (Core Study) and Months 24-48 (Extension Study)
Measure Description	ARR is defined as the number of confirmed relapses in a year. A relapse is defined as the appearance of a new or worsening of a previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding relapse. The abnormality must be present for at least 24 hours and occur in the absence of fever or infection. The annualized ARR for each treatment group was the mean of the annualized ARRs for all patients in the group, calculated as the total number of confirmed relapses divided by the total number of days on study multiplied by 365.25.

Time Frame	Months 0-24 (core study) and Months 24-48 (extension study)
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.
Extension intent-to-treat (ITT) population: All extension randomized patients that received at least 1 dose of extension study drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod 1.25 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 1.25 mg/day in this extension study.
Placebo-fingolimod 0.5 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 0.5 mg/day in this extension study.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo-fingolimod 1.25 mg**	**Placebo-fingolimod 0.5 mg**
Number of Participants Analyzed [units: participants]	**287**	**330**	**145**	**154**
Annualized Aggregate Relapse Rate (ARR) During Months 0-24 (Core Study) and Months 24-48 (Extension Study) [units: Relapses per year] Number (95% Confidence Interval)				

Months 0-24	**0.064 (0.043 to 0.094)**	**0.111 (0.084 to 0.148)**	**0.301 (0.230 to 0.393)**	**0.292 (0.222 to 0.383)**
Months 24-48	**0.074 (0.051 to 0.108)**	**0.095 (0.070 to 0.128)**	**0.164 (0.117 to 0.231)**	**0.130 (0.092 to 0.184)**

No statistical analysis provided for Annualized Aggregate Relapse Rate (ARR) During Months 0-24 (Core Study) and Months 24-48 (Extension Study)

4. Primary: Change (Expressed as Ratio) in the Annualized Aggregate Relapse Rate (ARR) From Months 0-24 (Core Study) to Months 24-48 (Extension Study) [Time Frame: Months 0-24 (core study) and Months 24-48 (extension study)]

Measure Type	Primary
Measure Title	Change (Expressed as Ratio) in the Annualized Aggregate Relapse Rate (ARR) From Months 0-24 (Core Study) to Months 24-48 (Extension Study)
Measure Description	ARR is defined as the number of confirmed relapses in a year. A relapse is defined as the appearance of a new or worsening of a previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding relapse. The abnormality must be present for at least 24 hours and occur in the absence of fever or infection. The annualized ARR for each treatment group was the mean of the annualized ARRs for all patients in the group, calculated as the total number of confirmed relapses divided by the total number of days on study multiplied by 365.25.
Time Frame	Months 0-24 (core study) and Months 24-48 (extension study)
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.
Extension intent-to-treat (ITT) population: All extension randomized patients that received at least 1 dose of extension study drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod 1.25 mg	Patients randomized to placebo in the Core study were re-randomized to fingolimod 1.25 mg/day in this extension study.
Placebo-fingolimod 0.5 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 0.5 mg/day in this extension study.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo-fingolimod 1.25 mg	Placebo-fingolimod 0.5 mg
Number of Participants Analyzed [units: participants]	**287**	**330**	**145**	**154**
Change (Expressed as Ratio) in the Annualized Aggregate Relapse Rate (ARR) From Months 0-24 (Core Study) to Months 24-48 (Extension Study) [units: Ratio of relapses per year] Number (95% Confidence Interval)	**1.164 (0.830 to 1.633)**	**0.850 (0.658 to 1.099)**	**0.547 (0.390 to 0.767)**	**0.446 (0.320 to 0.620)**

No statistical analysis provided for Change (Expressed as Ratio) in the Annualized Aggregate Relapse Rate (ARR) From Months 0-24 (Core Study) to Months 24-48 (Extension Study)

5. Secondary: Change in Mean Number of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study) [Time Frame: Months 0-24 (core study) and Months 24-48 (extension study)]

Measure Type	Secondary
Measure Title	Change in Mean Number of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study)
Measure Description	The number of new or newly enlarged T2 lesions was assessed with T2-weighted MRI scans. A T2-weighted MRI scan utilizes particular values of the echo time (TE) and the repetition time (TR) parameters of image acquisition. Inflammation and tissue damage are seen as bright areas in T2 images and are often referred to as T2 lesions. T2 weighted MRI scans are a sensitive way to evaluate the brain for demyelinating diseases, such as multiple sclerosis.
Time Frame	Months 0-24 (core study) and Months 24-48 (extension study)
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.
Extension intent-to-treat (ITT) population: All extension randomized patients that received at least 1 dose of extension study drug. The analysis included number of patients with evaluable T2 MRI scans.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod 1.25 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 1.25 mg/day in this extension study.
Placebo-fingolimod 0.5 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 0.5 mg/day in this extension study.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo-fingolimod 1.25 mg	Placebo-fingolimod 0.5 mg
Number of Participants Analyzed [units: participants]	**123**	**163**	**64**	**69**
Change in Mean Number of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study) [units: Lesions] Mean (Standard Deviation)				
Months 0-24	**2.14 (5.234)**	**2.66 (9.395)**	**12.83 (17.573)**	**8.12 (11.083)**
Months 24-48	**1.71 (4.902)**	**2.58 (9.256)**	**2.34 (4.745)**	**1.43 (2.446)**
Change from Months 0-24 to Months 24-48	**-0.43 (4.393)**	**-0.09 (7.423)**	**-10.48 (15.980)**	**-6.68 (9.876)**

No statistical analysis provided for Change in Mean Number of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study)

6. Secondary: Percentage of Patients Free of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study) [Time Frame: Months 0-24 (core study) and Months 24-48 (extension study)]

Measure Type	Secondary
Measure Title	Percentage of Patients Free of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study)
Measure Description	The number of new or newly enlarged T2 lesions was assessed with T2-weighted MRI scans. A T2-weighted MRI scan utilizes particular values of the echo time (TE) and the repetition time (TR) parameters of image acquisition. Inflammation and tissue damage are seen as bright areas in T2 images and are often referred to as T2 lesions. T2 weighted MRI scans are a sensitive way to evaluate the brain for demyelinating diseases, such as multiple sclerosis.

Time Frame	Months 0-24 (core study) and Months 24-48 (extension study)
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.
Extension intent-to-treat (ITT) population: All extension randomized patients that received at least 1 dose of extension study drug. The analysis included number of patients with evaluable T2 MRI scans.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod 1.25 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 1.25 mg/day in this extension study.
Placebo-fingolimod 0.5 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 0.5 mg/day in this extension study.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo-fingolimod 1.25 mg	Placebo-fingolimod 0.5 mg
Number of Participants Analyzed [units: participants]	**126**	**163**	**65**	**69**
Percentage of Patients Free of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study)				

[units: Percentage of patients]				
Months 0-24	**53.2**	**50.3**	**18.5**	**23.2**
Months 24-48	**57.1**	**69.3**	**52.3**	**55.1**

No statistical analysis provided for Percentage of Patients Free of New or Newly Enlarged T2 Magnetic Resonance Imaging (MRI) Lesions During Months 0-24 (Core Study) and Months 24-48 (Extension Study)

7. Secondary: Percent Change in Brain Volume From Month 0 to Month 24 (Core Study) and From Month 24 to Month 48 (Extension Study) [Time Frame: Months 0-24 (core study) and Months 24-48 (extension study)]

Measure Type	Secondary
Measure Title	Percent Change in Brain Volume From Month 0 to Month 24 (Core Study) and From Month 24 to Month 48 (Extension Study)
Measure Description	Calculations of brain volume change were performed using the structural image evaluation of normalized atrophy (SIENA), software included in the Functional Magnetic Resonance Imaging of the Brain (FMRIB) software library. SIENA is a fully automated method for estimating temporal brain volume change.
Time Frame	Months 0-24 (core study) and Months 24-48 (extension study)
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.
Extension intent-to-treat (ITT) population: All extension randomized patients that received at least 1 dose of extension study drug.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25

	mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod 1.25 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 1.25 mg/day in this extension study.
Placebo-fingolimod 0.5 mg	Patients randomized to placebo in the core study were re-randomized to fingolimod 0.5 mg/day in this extension study.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo-fingolimod 1.25 mg	Placebo-fingolimod 0.5 mg
Number of Participants Analyzed [units: participants]	**287**	**330**	**145**	**154**
Percent Change in Brain Volume From Month 0 to Month 24 (Core Study) and From Month 24 to Month 48 (Extension Study) [units: Percent change] Mean (Standard Deviation)				
Month 0 to Month 24, n=75, 109, 41, 49	**-1.011 (1.3477)**	**-0.983 (1.6291)**	**-1.511 (1.6401)**	**-1.419 (1.3923)**
Month 24 to Month 48, n=75, 109, 41, 49	**-0.871 (1.4164)**	**-0.780 (1.9266)**	**-1.103 (1.4073)**	**-0.903 (1.1406)**

No statistical analysis provided for Percent Change in Brain Volume From Month 0 to Month 24 (Core Study) and From Month 24 to Month 48 (Extension Study)

8. Secondary: Percent Change in Brain Volume From Month 0 End of Study (Core and Extension Study) [Time Frame: Months 0 to end of study (maximum up to 60 months)]

Measure Type	Secondary
Measure Title	Percent Change in Brain Volume From Month 0 End of Study (Core and Extension Study)
Measure Description	Calculations of brain volume change were performed using the structural image evaluation of normalized atrophy (SIENA), software included in the Functional Magnetic Resonance Imaging of the Brain (FMRIB) software library. SIENA is a fully automated method for estimating temporal brain volume change.
Time Frame	Months 0 to end of study (maximum up to 60 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 study and received at least 1 dose of Core study drug. This analysis included only patients with value at both core baseline and end of study.

Reporting Groups

	Description
Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod	Patients randomized to placebo in the Core study who were subsequently re-randomized to fingolimod (either 1.25 or 0.5 mg/day) in the Extension study.

Measured Values

	Fingolimod 1.25 mg	**Fingolimod 0.5 mg**	**Placebo-fingolimod**
Number of Participants Analyzed [units: participants]	**250**	**299**	**259**

Percent Change in Brain Volume From Month 0 End of Study (Core and Extension Study) [units: Percent change] Mean (Standard Deviation)	**-1.639 (1.9265)**	**-1.674 (2.1182)**	**-2.241 (2.1873)**

No statistical analysis provided for Percent Change in Brain Volume From Month 0 End of Study (Core and Extension Study)

9. Secondary: Time to First 3-month Confirmed Disability Progression up to End of Study Based on Expanded Disability Status Scale (EDSS): Kaplan-Meier Estimate of Percentage of Patients Free of Disability Progression [Time Frame: Core baseline to end of study (maximum up to 60 months)]

Measure Type	Secondary
Measure Title	Time to First 3-month Confirmed Disability Progression up to End of Study Based on Expanded Disability Status Scale (EDSS): Kaplan-Meier Estimate of Percentage of Patients Free of Disability Progression
Measure Description	Kurtzke's Expanded Disability Status Scale (EDSS) is a scale for assessing neurologic impairment in multiple sclerosis (MS) includes a series of scores in each of eight functional systems such as Visual, Brain Stem, Pyramidal, Cerebellar, Sensory, Bowel & Bladder, Cerebral, and Other. The EDSS steps range from 0 (normal) to 10 (death due to MS). The Kaplan-Meier estimates of the percentage of participants free of disability progression at end of study and their 95% CIs were provided for each treatment group.
Time Frame	Core baseline to end of study (maximum up to 60 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 study and received at least 1 dose of Core study drug.

Reporting Groups

	Description

Fingolimod 1.25 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 1.25 mg/day, in this extension study.
Fingolimod 0.5 mg	Patients continued the same dose to which they had been randomized in the core study, fingolimod 0.5 mg/day, in this extension study.
Placebo-fingolimod	Patients randomized to placebo in the Core study who were subsequently re-randomized to fingolimod(either 1.25 or 0.5 mg/day) in the Extension study.

Measured Values

	Fingolimod 1.25 mg	Fingolimod 0.5 mg	Placebo-fingolimod
Number of Participants Analyzed [units: participants]	**429**	**425**	**418**
Time to First 3-month Confirmed Disability Progression up to End of Study Based on Expanded Disability Status Scale (EDSS): Kaplan-Meier Estimate of Percentage of Patients Free of Disability Progression [units: Percentage of patients] Number (95% Confidence Interval)	**74.15 (69.54 to 78.75)**	**73.90 (69.44 to 78.37)**	**66.28 (61.28 to 71.28)**

No statistical analysis provided for Time to First 3-month Confirmed Disability Progression up to End of Study Based on Expanded Disability Status Scale (EDSS): Kaplan-Meier Estimate of Percentage of Patients Free of Disability Progression

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	Safety reported on extension safety population which includes all patients who received at least 1 dose of Extension study drug. Patients were analyzed according to the actual treatment received during extension.

Reporting Groups

	Description
Fingolimod 1.25mg	Patients randomized to fingolimod 1.25 mg/day in the Core study. These patients continued the same dose in the Extension study.
Fingolimod 0.5mg	Patients randomized to fingolimod 0.5 mg/day in the Core study. These patients continued the same dose in the Extension study.
Placebo-Fingolimod 1.25mg	Patients randomized to placebo in the Core study who were subsequently re-randomized to fingolimod 1.25 mg/day in the Extension study.
Placebo-Fingolimod 0.5mg	Patients randomized to placebo in the Core study who were subsequently re-randomized to fingolimod 0.5 mg/day in the Extension study.

Serious Adverse Events

	Fingolimod 1.25mg	Fingolimod 0.5mg	Placebo-Fingolimod 1.25mg	Placebo-Fingolimod 0.5mg
Total, serious adverse events				
# participants affected / at risk	**31/289 (10.73%)**	**31/331 (9.37%)**	**17/145 (11.72%)**	**11/155 (7.10%)**
Blood and lymphatic system disorders				
Lymphopenia † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Thrombocytopenia † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Cardiac disorders				
Acute myocardial infarction † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Angina pectoris † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**

Atrioventricular block complete † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Atrioventricular block second degree † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Atrioventricular extrasystoles † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Bradyarrhythmia † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Bradycardia † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Palpitations † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Sinus bradycardia † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Supraventricular tachycardia † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Congenital, familial and genetic disorders				
Dermoid cyst † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Endocrine disorders				
Thyroid cyst † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Eye disorders				
Retinal detachment † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**

Gastrointestinal disorders				
Abdominal pain † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Gastritis † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Irritable bowel syndrome † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Rectal haemorrhage † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
General disorders				
Fatigue † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Hepatobiliary disorders				
Cholelithiasis † 1				
# participants affected / at risk	**2/289 (0.69%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Infections and infestations				
Appendicitis † 1				
# participants affected / at risk	**1/289 (0.35%)**	**2/331 (0.60%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Borrelia infection † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Bronchitis † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Cellulitis † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Gastroenteritis viral † 1				

# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Genital infection † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Herpes zoster † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Herpes zoster oticus † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Influenza † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Lobar pneumonia † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Lymphangitis † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Pyelonephritis † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Salpingo-oophoritis † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	1/155 (0.65%)
Tracheitis † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Urinary tract infection † 1				
# participants affected / at risk	1/289 (0.35%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Injury, poisoning and procedural complications				
Crush injury † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)

Hand fracture † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Injury † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Limb injury † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Lower limb fracture † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Overdose † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Radius fracture † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Subdural haematoma † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Investigations				
Alanine aminotransferase increased † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Aspartate aminotransferase increased † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Musculoskeletal and connective tissue disorders				
Back pain † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**1/155 (0.65%)**
Intervertebral disc protrusion † 1				
# participants affected / at risk	**1/289 (0.35%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Osteoarthritis † 1				

# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Osteochondrosis † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Pain in extremity † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Basal cell carcinoma † 1				
# participants affected / at risk	2/289 (0.69%)	3/331 (0.91%)	2/145 (1.38%)	0/155 (0.00%)
Benign lung neoplasm † 1				
# participants affected / at risk	0/289 (0.00%)	0/331 (0.00%)	1/145 (0.69%)	0/155 (0.00%)
Benign ovarian tumour † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Borderline ovarian tumour † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Cervix carcinoma stage 0 † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Fibroadenoma of breast † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Malignant melanoma † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	1/155 (0.65%)
Malignant neoplasm of eyelid † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Melanocytic naevus † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)

Meningioma benign † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Uterine leiomyoma † 1				
# participants affected / at risk	**0/289 (0.00%)**	**2/331 (0.60%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Nervous system disorders				
Convulsion † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Epilepsy † 1				
# participants affected / at risk	**0/289 (0.00%)**	**2/331 (0.60%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Migraine † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Multiple sclerosis relapse † 1				
# participants affected / at risk	**3/289 (1.04%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Nerve compression † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Neuralgia † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Presyncope † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Sciatica † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Status epilepticus † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**1/155 (0.65%)**
Syncope † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**

Transient ischaemic attack † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Psychiatric disorders				
Acute psychosis † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Depression † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**2/145 (1.38%)**	**0/155 (0.00%)**
Paranoia † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Personality disorder † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Psychotic disorder † 1				
# participants affected / at risk	**0/289 (0.00%)**	**1/331 (0.30%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Suicide attempt † 1				
# participants affected / at risk	**0/289 (0.00%)**	**0/331 (0.00%)**	**1/145 (0.69%)**	**0/155 (0.00%)**
Renal and urinary disorders				
Urethral stenosis † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Reproductive system and breast disorders				
Breast mass † 1				
# participants affected / at risk	**1/289 (0.35%)**	**0/331 (0.00%)**	**0/145 (0.00%)**	**0/155 (0.00%)**
Metrorrhagia † 1				

# participants affected / at risk	0/289 (0.00%)	0/331 (0.00%)	0/145 (0.00%)	1/155 (0.65%)
Respiratory, thoracic and mediastinal disorders				
Dysphonia † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Dyspnoea † 1				
# participants affected / at risk	0/289 (0.00%)	0/331 (0.00%)	1/145 (0.69%)	0/155 (0.00%)
Hyperventilation † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Snoring † 1				
# participants affected / at risk	0/289 (0.00%)	0/331 (0.00%)	0/145 (0.00%)	1/155 (0.65%)
Skin and subcutaneous tissue disorders				
Lymphomatoid papulosis † 1				
# participants affected / at risk	0/289 (0.00%)	0/331 (0.00%)	1/145 (0.69%)	0/155 (0.00%)
Parapsoriasis † 1				
# participants affected / at risk	0/289 (0.00%)	0/331 (0.00%)	1/145 (0.69%)	0/155 (0.00%)
Surgical and medical procedures				
Selective abortion † 1				
# participants affected / at risk	1/289 (0.35%)	0/331 (0.00%)	0/145 (0.00%)	0/155 (0.00%)
Vascular disorders				
Hypertension † 1				
# participants affected / at risk	0/289 (0.00%)	1/331 (0.30%)	0/145 (0.00%)	0/155 (0.00%)
Vascular stenosis † 1				
# participants affected / at risk	0/289 (0.00%)	0/331 (0.00%)	1/145 (0.69%)	0/155 (0.00%)

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

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	Safety reported on extension safety population which includes all patients who received at least 1 dose of Extension study drug. Patients were analyzed according to the actual treatment received during extension.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Fingolimod 1.25mg	Patients randomized to fingolimod 1.25 mg/day in the Core study. These patients continued the same dose in the Extension study.
Fingolimod 0.5mg	Patients randomized to fingolimod 0.5 mg/day in the Core study. These patients continued the same dose in the Extension study.
Placebo-Fingolimod 1.25mg	Patients randomized to placebo in the Core study who were subsequently re-randomized to fingolimod 1.25 mg/day in the Extension study.
Placebo-Fingolimod 0.5mg	Patients randomized to placebo in the Core study who were subsequently re-randomized to fingolimod 0.5 mg/day in the Extension study.

Other Adverse Events

	Fingolimod 1.25mg	Fingolimod 0.5mg	Placebo-Fingolimod 1.25mg	Placebo-Fingolimod 0.5mg
Total, other (not including serious) adverse events				

# participants affected / at risk	**236/289 (81.66%)**	**273/331 (82.48%)**	**107/145 (73.79%)**	**130/155 (83.87%)**
Blood and lymphatic system disorders				
Lymphopenia † 1				
# participants affected / at risk	**52/289 (17.99%)**	**52/331 (15.71%)**	**18/145 (12.41%)**	**17/155 (10.97%)**
Gastrointestinal disorders				
Diarrhoea † 1				
# participants affected / at risk	**14/289 (4.84%)**	**29/331 (8.76%)**	**10/145 (6.90%)**	**10/155 (6.45%)**
General disorders				
Fatigue † 1				
# participants affected / at risk	**12/289 (4.15%)**	**23/331 (6.95%)**	**7/145 (4.83%)**	**8/155 (5.16%)**
Infections and infestations				
Bronchitis † 1				
# participants affected / at risk	**19/289 (6.57%)**	**20/331 (6.04%)**	**10/145 (6.90%)**	**11/155 (7.10%)**
Cystitis † 1				
# participants affected / at risk	**7/289 (2.42%)**	**12/331 (3.63%)**	**8/145 (5.52%)**	**3/155 (1.94%)**
Gastroenteritis † 1				
# participants affected / at risk	**15/289 (5.19%)**	**11/331 (3.32%)**	**3/145 (2.07%)**	**5/155 (3.23%)**
Influenza † 1				
# participants affected / at risk	**30/289 (10.38%)**	**33/331 (9.97%)**	**9/145 (6.21%)**	**12/155 (7.74%)**
Nasopharyngitis † 1				
# participants affected / at risk	**82/289 (28.37%)**	**84/331 (25.38%)**	**39/145 (26.90%)**	**44/155 (28.39%)**
Oral herpes † 1				

# participants affected / at risk	19/289 (6.57%)	24/331 (7.25%)	10/145 (6.90%)	11/155 (7.10%)
Pharyngitis † 1				
# participants affected / at risk	14/289 (4.84%)	17/331 (5.14%)	8/145 (5.52%)	5/155 (3.23%)
Sinusitis † 1				
# participants affected / at risk	8/289 (2.77%)	15/331 (4.53%)	7/145 (4.83%)	10/155 (6.45%)
Upper respiratory tract infection † 1				
# participants affected / at risk	39/289 (13.49%)	58/331 (17.52%)	23/145 (15.86%)	24/155 (15.48%)
Urinary tract infection † 1				
# participants affected / at risk	20/289 (6.92%)	27/331 (8.16%)	12/145 (8.28%)	8/155 (5.16%)
Investigations				
Alanine aminotransferase increased † 1				
# participants affected / at risk	10/289 (3.46%)	11/331 (3.32%)	16/145 (11.03%)	9/155 (5.81%)
Carbon monoxide diffusing capacity decreased † 1				
# participants affected / at risk	21/289 (7.27%)	16/331 (4.83%)	10/145 (6.90%)	9/155 (5.81%)
Gamma-glutamyltransferase increased † 1				
# participants affected / at risk	7/289 (2.42%)	8/331 (2.42%)	12/145 (8.28%)	8/155 (5.16%)
Lymphocyte count decreased † 1				
# participants affected / at risk	29/289 (10.03%)	16/331 (4.83%)	12/145 (8.28%)	14/155 (9.03%)
Weight decreased † 1				
# participants affected / at risk	3/289 (1.04%)	6/331 (1.81%)	4/145 (2.76%)	12/155 (7.74%)
Metabolism and nutrition disorders				
Hypercholesterolaemia † 1				
# participants affected / at risk	18/289 (6.23%)	24/331 (7.25%)	7/145 (4.83%)	13/155 (8.39%)
Musculoskeletal and connective tissue disorders				

Arthralgia † [1]				
# participants affected / at risk	**20/289 (6.92%)**	**21/331 (6.34%)**	**6/145 (4.14%)**	**8/155 (5.16%)**
Back pain † [1]				
# participants affected / at risk	**20/289 (6.92%)**	**21/331 (6.34%)**	**12/145 (8.28%)**	**14/155 (9.03%)**
Pain in extremity † [1]				
# participants affected / at risk	**15/289 (5.19%)**	**18/331 (5.44%)**	**9/145 (6.21%)**	**8/155 (5.16%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Melanocytic naevus † [1]				
# participants affected / at risk	**22/289 (7.61%)**	**16/331 (4.83%)**	**4/145 (2.76%)**	**4/155 (2.58%)**
Skin papilloma † [1]				
# participants affected / at risk	**15/289 (5.19%)**	**10/331 (3.02%)**	**5/145 (3.45%)**	**3/155 (1.94%)**
Nervous system disorders				
Dizziness † [1]				
# participants affected / at risk	**7/289 (2.42%)**	**7/331 (2.11%)**	**6/145 (4.14%)**	**10/155 (6.45%)**
Headache † [1]				
# participants affected / at risk	**27/289 (9.34%)**	**41/331 (12.39%)**	**18/145 (12.41%)**	**26/155 (16.77%)**
Respiratory, thoracic and mediastinal disorders				
Cough † [1]				
# participants affected / at risk	**19/289 (6.57%)**	**27/331 (8.16%)**	**13/145 (8.97%)**	**11/155 (7.10%)**
Vascular disorders				
Hypertension † [1]				
# participants affected / at risk	**24/289 (8.30%)**	**18/331 (5.44%)**	**13/145 (8.97%)**	**15/155 (9.68%)**

† 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:** ☑ 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. 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 (ie, 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

Responsible Party:	Novartis
ClinicalTrials.gov Identifier:	NCT00662649 History of Changes
Other Study ID Numbers:	**CFTY720D2301E1** 2007-004122-24 (EudraCT Number)
Study First Received:	April 17, 2008
Results First Received:	June 9, 2012
Last Updated:	June 9, 2012
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