

Protocol Registration and Results System

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Results Preview

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Participant Flow

Recruitment Details	
Pre-Assignment Details	

Arm/Group Title	Fampridine	Total (Not public)
▼ Arm/Group Description	All participants took 10 mg fampridine twice daily for the first 4 weeks. If deemed a treatment responder, the participant continued 10 mg fampridine twice daily for 44 weeks. Treatment non-responders continued without treatment by completing quality of life questionnaires.	
Period Title: Overall Study		
Started	901 [1]	901
Intent to Treat Population	835 [2]	835
Completed	611	611
Not Completed	290	290
Reason Not Completed		
Run-in Failure	52	52
Adverse Event	39	39
Death	2	2
Disease Progression	5	5
Non-compliance With Study Protocol	15	15
Withdrawal by Subject	105	105
Lost to Follow-up	7	7
Investigator Decision	13	13
Not Specified	52	52
(Not Public)	Not Completed =290 Total from all reasons =290	
[1] enrolled and started run-in treatment		
[2] Received ≥4 doses of study drug & provided ≥4 efficacy assessment at Baseline & the 2-month		

▶ **Baseline Characteristics**

Arm/Group Title ▼ Arm/Group Description		Responder	Non-responder	Total
		Participants took 10 mg fampridine twice daily for the first 4 weeks. If deemed a treatment responder, the participant continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Treatment non-responders continued without treatment by completing quality of life questionnaires.	
Overall Number of Baseline Participants ▼ Baseline Analysis Population Description		707	128	835
		Intent-to-treat population: all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit.		
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	707 participants	128 participants	835 participants
		49.3 (9.70)	50.5 (10.0)	49.5 (9.75)
Gender, Male/Female Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	707 participants	128 participants	835 participants
	Female	402 56.86%	79 61.72%	481 57.6%
	Male	305 43.14%	49 38.28%	354 42.4%

▶ **Outcome Measures**

1. Primary Outcome

Title:	Change From Baseline in the Physical Component Scale (PCS) of the Short Form 36 Health Status Questionnaire (SF-36) At Months 3, 6, 9, and 12: Responders
▼ Description:	The SF-36 determines participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 primarily contribute to

	the PCS score of the SF-36. Items 5-8 primarily contribute to the mental component summary (MCS) score of the SF-36. Scores on each item are summed and averaged (range: 0=worst to 100=best). Increases from baseline indicate improvement. Within-group least squares means are presented.
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	666
Least Squares Mean (Standard Error) Unit of measure: units on a scale	
Row Title: Month 3	4.2 (0.36)
Row Title: Month 6	3.4 (0.38)
Row Title: Month 9	3.2 (0.37)
Row Title: Month 12	2.9 (0.37)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3: Mixed effect model for repeated measures with visit,

		baseline PCS score, baseline Expanded Disability Status Scale (EDSS) score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	within group p-value
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6: Mixed effect model for repeated measures with visit, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	within group p-value
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

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Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Difference of Month 3 versus Month 6: Mixed effect model for repeated measures with visit, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0007
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.22
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9: Mixed effect model for repeated measures with visit, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	within-group p-value
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Difference of Month 6 versus Month 9: Mixed effect model for repeated measures with visit, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2531
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.21
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 12: Mixed effect model for repeated measures with visit, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	within group p-value
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Difference of Month 9 versus Month 12: Mixed effect model for repeated measures with visit, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2299
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.21
	Estimation Comments	[Not specified]

2. Secondary Outcome

Title:	Change From Baseline in the PCS of the SF-36 at Months 3, 6, 9, and 12: Responders Versus Non-responders
▼ Description:	The SF-36 determines participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 primarily contribute to the PCS score of the SF-36. Items 5-8 primarily contribute to the MCS score of the SF-36. Scores on each item are summed and averaged (range: 0=worst to 100=best). Increases from baseline indicate improvement. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12). In contrast to the primary endpoint, this analysis was done using data from both responder and non-responder groups; therefore, 'responder group' and 'visit by responder group interaction' were included as fixed effects.
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	666	81

Least Squares Mean (Standard Error) Unit of measure: units on a scale		
Row Title: Overall	3.3 (0.34)	-0.4 (0.63)
Row Title: Month 3	4.0 (0.36)	-0.2 (0.67)
Row Title: Month 6	3.3 (0.37)	0.2 (0.77)
Row Title: Month 9	3.0 (0.37)	-1.1 (0.80)
Row Title: Month 12	2.8 (0.37)	-0.5 (0.81)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total

		number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5405
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of	Estimation Parameter	Other[least squares mean]

Estimation	Estimated Value	3.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.58
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An

		unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7272
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	4.3
	Parameter Dispersion	Type: Standard Error of the mean

		Value: 0.64
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7484
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	3.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.75
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1877
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	4.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.78
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.5460

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline PCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	3.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.79
	Estimation Comments	[Not specified]

3. Secondary Outcome

Title:	Change From Baseline in the MCS of the SF-36 At Months 3, 6, 9, and 12
▼ Description:	The SF-36 determines participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in

	usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 primarily contribute to the PCS score of the SF-36. Items 5-8 primarily contribute to the MCS score of the SF-36. Scores on each item are summed and averaged (range: 0=worst to 100=best). Increases from baseline indicate improvement. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	667	81
Least Squares Mean (Standard Error) Unit of measure: units on a scale		
Row Title: Overall	3.1 (0.53)	0.1 (0.95)
Row Title: Month 3	4.2 (0.55)	-0.6 (1.03)
Row Title: Month 6	3.3 (0.56)	0.6 (1.12)
Row Title: Month 9	2.3 (0.58)	1.0 (1.22)
Row Title: Month 12	2.5 (0.57)	-0.6 (1.21)

▼ Statistical Analysis 1

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.9073
	Comments	[Not specified]

Hypothesis		
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0009
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	3.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.89
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder

		status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5542
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	4.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.99
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total

		number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5810
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

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Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0140
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	2.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.08
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4138
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect

		model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2740
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	1.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.19
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6453
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MCS score, baseline

		EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0090
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	3.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.18
	Estimation Comments	[Not specified]

4. Secondary Outcome

Title:	Change From Baseline in the Multiple Sclerosis Impact Scale (MSIS-29) Physical Score at Months 3, 6, 9, and 12
▼ Description:	The MSIS-29 is a disease specific patient-reported outcome measure that has been developed and validated to examine the physical and psychological impact of MS from a patient's perspective; it measures 20 physical items and 9 psychological items. Sum of 20 physical condition items converted into a 0-100 score range, where missing items are imputed by average of total of non-missing items when no more than 50% are missing (otherwise the total score is missing). A lower total score indicates less physically-related impact while a higher total score indicates greater physically-related impact on a participant's functioning. Decreases from Baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	669	79
Least Squares Mean (Standard Error) Unit of measure: units on a scale		
Row Title: Overall	-10.3 (0.99)	-2.1 (1.79)
Row Title: Month 3	-13.0 (1.00)	-2.1 (1.83)
Row Title: Month 6	-10.6 (1.03)	-3.0 (1.99)
Row Title: Month 9	-8.9 (1.06)	-0.3 (2.19)
Row Title: Month 12	-8.6 (1.06)	-2.8 (2.23)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2475
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-8.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.66
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2422
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-10.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.72
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.1262

Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-7.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.90
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed effect model for repeated

		measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8858
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-8.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.12
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29

		physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2111
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 physical score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0072
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-5.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.16
	Estimation Comments	[Not specified]

5. Secondary Outcome

Title:	Change From Baseline in MSIS-29 Psychological Score at Months 3, 6, 9, and 12
▼ Description:	The MSIS-29 is a disease specific patient-reported outcome measure that has been developed and validated to examine the physical and psychological impact of MS from a patient's perspective; it measures 20 physical items and 9 psychological items. Sum of 9 psychological condition items converted into a 0-100 score range, where missing items are imputed

	by average of total of non-missing items when no more than 50% are missing (otherwise the total score is missing). A lower total score indicates less psychologically-related impact while a higher total score indicates greater psychologically-related impact on a participant's functioning. Decreases from Baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	669	79
Least Squares Mean (Standard Error) Unit of measure: units on a scale		
Row Title: Overall	-7.8 (0.97)	-1.0 (1.77)
Row Title: Month 3	-9.6 (1.01)	-0.2 (1.91)
Row Title: Month 6	-7.7 (1.03)	-2.6 (2.06)
Row Title: Month 9	-6.8 (1.06)	-0.8 (2.26)
Row Title: Month 12	-7.0 (1.06)	-0.5 (2.34)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction,

		baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5577
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-6.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.64
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type,

		age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9365
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

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Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-9.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.82
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as

		fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2008
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus

		Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0102
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-5.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.98
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model

		within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7134
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures

		with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0066
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-6.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.20
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8202
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder status, visit by responder status interaction, baseline MSIS-29 psychological

		score, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0049
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-6.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.28
	Estimation Comments	[Not specified]

6. Secondary Outcome

Title:	Change From Baseline in the Activities Limitation Scale of the Patient-Reported Indices for Multiple Sclerosis (PRIMUS) at Months 3, 6, 9, and 12
▼ Description:	The PRIMUS activity measure is a 15-item assessment of patient-reported activities of daily living. The total score was calculated as sum of all 15 items converted into a 0-30 range, where missing items were imputed by average of non-missing total when no more than 50% of items were missing (otherwise, the total score is missing). Higher score indicates worse condition. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	498	45
Least Squares Mean (Standard Error) Unit of measure: units on a scale		
Row Title: Overall	-1.4 (0.22)	0.8 (0.56)
Row Title: Month 3	-2.3 (0.23)	-0.4 (0.58)
Row Title: Month 6	-1.4 (0.25)	0.8 (0.70)
Row Title: Month 9	-1.2 (0.25)	1.8 (0.73)
Row Title: Month 12	-0.8 (0.26)	1.1 (0.83)

▼ Statistical Analysis 1

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1324
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-2.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.56
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4759
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0016
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-1.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.59
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2489
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0017
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-2.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.71
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0126
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-3.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.75
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0033
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1758
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the total activity limitation score of PRIMUS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0246
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-1.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.84
	Estimation Comments	[Not specified]

7. Secondary Outcome

Title:	Change From Baseline in the Current Health State of EuroQoL Descriptive System of Health-related Quality of Life States Consisting of 5 Dimensions (EQ-5D) Visual Analog Scale (VAS) at Months 3, 6, 9, And 12
▼ Description:	EQ-5D is a participant-answered questionnaire containing a descriptive system of 5 dimensions - mobility, self-care, usual activities, pain/discomfort and anxiety/depression and a VAS on health state. The EQ-5D VAS ranges from 0 (worst health state) to 100 (best health state). An increase from baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	659	79
Least Squares Mean (Standard Error) Unit of measure: units on a scale		
Row Title: Overall	6.7 (0.95)	-4.4 (1.73)
Row Title: Month 3	8.0 (1.00)	-3.2 (1.91)
Row Title: Month 6	6.1 (1.02)	-3.6 (2.06)
Row Title: Month 9	6.3 (1.04)	-4.9 (2.21)
Row Title: Month 12	6.3 (1.05)	-6.0 (2.34)

▼ Statistical Analysis 1

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.0111

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder Versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	11.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.61
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed

		effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.0970

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder Versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	11.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.82
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6, Responder: Mixed

		effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.0789

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder Versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	9.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.00
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed

		effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.0284

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder Versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	11.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.16
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 12, Responder: Mixed

		effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.0108

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder Versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of the current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	12.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.29
	Estimation Comments	[Not specified]

8. Secondary Outcome

Title:	Change From Baseline in the Index Scores of EQ-5D at Months 3, 6, 9, and 12
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▼ Description:	EQ-5D is a participant-answered questionnaire containing a descriptive system on 5 dimensions - mobility, self-care, usual activities, pain/discomfort and anxiety/depression and a VAS on health state. The scores on the 5 dimensions of descriptive system can be converted into an index score by applying United Kingdom (UK) weights. EQ-5D index score ranges from 1 to -0.59, and 1 reflects the best outcome. An increase from baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	661	78
Least Squares Mean (Standard Error) Unit of measure: units on a scale		
Row Title: Overall	0.05 (0.01)	0.00 (0.02)
Row Title: Month 3	0.07 (0.01)	0.01 (0.02)
Row Title: Month 6	0.05 (0.01)	0.01 (0.02)
Row Title: Month 9	0.04 (0.01)	0.01 (0.03)
Row Title: Month 12	0.04 (0.01)	-0.01 (0.03)

▼ Statistical Analysis 1

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8392
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0162
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.04
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.02
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6956
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0042
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.06
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.02
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7949
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0679
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.04
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.02
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0027
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8053
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2638
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.03
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.03
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0007
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8502
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of current health state of EQ-5D scores, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0917
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.05
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.03
	Estimation Comments	[Not specified]

9. Secondary Outcome

Title:	Change From Baseline in Percent Work Time Missed Due to MS, by the
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	Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP) Questionnaire at Months 3, 6, 9, and 12
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	191	14
Least Squares Mean (Standard Error) Unit of measure: percentage of work time missed		
Row Title: Overall	-2.5 (1.87)	-8.3 (4.60)
Row Title: Month 3	-3.0 (2.15)	-4.0 (5.81)
Row Title: Month 6	-5.3 (1.95)	-7.6 (5.07)
Row Title: Month 9	-1.1 (2.31)	-9.6 (7.77)
Row Title: Month 12	-0.7 (2.24)	-12.1 (6.54)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1795
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0715
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2065
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	5.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.60
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical	Comparison Groups	Responder
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Analysis Overview	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1649
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4894
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8611
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	1.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.89
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0073
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1343
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6468
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	2.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.09
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6441
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2176
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2814
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	8.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.91
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis	Comparison Groups	Responder

Overview	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7533
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0653
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage of work time missed due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0876
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	11.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.65
	Estimation Comments	[Not specified]

10. Secondary Outcome

Title:	Change From Baseline in Percent Impairment While Working Due to MS, by
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	the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	217	16
Least Squares Mean (Standard Error) Unit of measure: percentage of impairment while working		
Row Title: Overall	-4.2 (1.88)	-8.4 (4.56)
Row Title: Month 3	-6.9 (2.09)	-1.8 (5.53)
Row Title: Month 6	-6.5 (2.01)	-5.6 (5.38)
Row Title: Month 9	-3.0 (2.18)	-17.9 (6.80)
Row Title: Month 12	-0.3 (2.22)	-8.4 (6.80)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0281
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0654
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3400
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	4.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.47
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0012
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7490
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3592
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-5.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.53
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0015
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2967
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8735
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-0.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.34
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1696
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0089
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0297
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	14.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.83
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8806
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2170
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage impairment while working due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2392
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	8.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.86
	Estimation Comments	[Not specified]

11. Secondary Outcome

Title:	Change From Baseline in Percent Overall Work Impairment Due to MS, by the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	186	13
Least Squares Mean (Standard Error) Unit of measure: percentage of overall work impairment		
Row Title: Overall	-5.2 (2.24)	-8.7 (5.69)
Row Title: Month 3	-7.7 (2.49)	-4.5 (6.57)
Row Title: Month 6	-7.8 (2.43)	-2.9 (6.73)
Row Title: Month 9	-2.4 (2.86)	-15.9 (9.83)
Row Title: Month 12	-2.9 (2.47)	-11.7 (7.06)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0219
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1259
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.5312
	Comments	[Not specified]
	Method	Other [mixed effect model]
Method of Estimation	Comments	[Not specified]
	Estimation Parameter	Other[least squares mean]
	Estimated Value	3.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.68

	Estimation Comments	[Not specified]
▼ Statistical Analysis 4 		
Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0022
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4968
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.6283
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-3.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.64

	Estimation Comments	[Not specified]
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▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0016
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6631
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.4770
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-4.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.77

	Estimation Comments	[Not specified]
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▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4027
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1077
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.1781
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	13.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 9.98

	Estimation Comments	[Not specified]
▼ Statistical Analysis 13 		
Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2422
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0994
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of percentage overall work impairment due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.2194
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	8.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.13

	Estimation Comments	[Not specified]
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12. Secondary Outcome

Title:	Change From Baseline in Regular Activity Productivity Loss, by the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder	Non-responder
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	650	77
Least Squares Mean (Standard Error) Unit of measure: percentage of activity impairment		
Row Title: Overall	-11.4 (1.31)	-4.1 (2.37)
Row Title: Month 3	-13.5 (1.42)	-3.1 (2.83)

Row Title: Month 6	-12.3 (1.43)	-4.7 (2.94)
Row Title: Month 9	-10.4 (1.44)	-4.1 (3.08)
Row Title: Month 12	-9.2 (1.45)	-4.4 (3.20)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Overall, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Overall, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An

		unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0860
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Overall, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0010
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-7.3

	Parameter Dispersion	Type: Standard Error of the mean Value: 2.20
	Estimation Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 3, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 3, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An

		unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2777
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 3, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-10.4

	Parameter Dispersion	Type: Standard Error of the mean Value: 2.76
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 6, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 6, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An

		unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1078
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 6, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0082
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-7.6

	Parameter Dispersion	Type: Standard Error of the mean Value: 2.87
	Estimation Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 9, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 9, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An

		unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1838
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 9, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0364
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-6.3

	Parameter Dispersion	Type: Standard Error of the mean Value: 3.02
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder
	Comments	Month 12, Responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder
	Comments	Month 12, Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An

		unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1714
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder, Non-responder
	Comments	Month 12, Responder versus Non-responder: Mixed effect model for repeated measures with visit, responder group, visit and responder group interaction, baseline of regular activity productivity loss due to MS, baseline EDSS score, MS disease type, age, gender, total number of relapses experienced within the past 12 months and country as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1259
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	-4.8

	Parameter Dispersion	Type: Standard Error of the mean Value: 3.14
	Estimation Comments	[Not specified]

13. Secondary Outcome

Title:	Change From Baseline in the PCS of the SF-36 at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	The SF-36 determines participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 primarily contribute to the PCS score of the SF-36. Items 5-8 primarily contribute to the MCS score of the SF-36. Scores on each item are summed and averaged (range: 0=worst to 100=best). Increases from baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those

	weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	256	264	115	31
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	4.5 (0.39)	3.8 (0.38)	2.5 (0.49)	3.2 (0.89)
Row Title: Month 3	5.5 (0.42)	4.5 (0.41)	3.1 (0.55)	2.7 (1.01)
Row Title: Month 6	4.4 (0.46)	3.9 (0.45)	2.3 (0.61)	3.9 (1.13)
Row Title: Month 9	4.2 (0.45)	3.2 (0.45)	3.0 (0.60)	3.2 (1.12)
Row Title: Month 12	4.0 (0.45)	3.4 (0.45)	1.7 (0.61)	2.9 (1.14)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	<0.0001

Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0004
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured

		covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0069
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country,

		visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical	Comparison Groups	Primary-Progressive MS
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Analysis Overview	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0006
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
Method	Method	Other [mixed effect model]
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0040
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced

		within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0047
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures

		with visit, baseline PCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0118
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

14. Secondary Outcome

Title:	Change From Baseline in the MCS of the SF-36 at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	The SF-36 determines participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 primarily contribute to the PCS score of the SF-36. Items 5-8 primarily contribute to the MCS score of the SF-36. Scores on each item are summed and averaged (range: 0=worst to 100=best). Increases from baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	256	264	116	31
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	4.0 (0.59)	3.0 (0.58)	3.2 (0.74)	2.0 (1.36)
Row Title: Month 3	4.9 (0.64)	4.5 (0.63)	3.9 (0.83)	2.6 (1.54)
Row Title: Month 6	4.3 (0.67)	2.9 (0.66)	3.5 (0.89)	2.9 (1.65)
Row Title: Month 9	3.1 (0.70)	2.1 (0.69)	2.7 (0.93)	2.0 (1.74)
Row Title: Month 12	3.5 (0.68)	2.6 (0.67)	2.5 (0.89)	0.5 (1.68)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as

		fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline MCS score,

		MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1398
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

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Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0935
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced

		within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0760
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures

		with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0019
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0037
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2489
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0052
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline MCS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7714
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

15. Secondary Outcome

Title:	Change From Baseline in the MSIS-29 Physical Score at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	The MSIS-29 is a disease-specific patient-reported outcome measure that has been developed and validated to examine the physical and psychological impact of MS from a patient's perspective; it measures 20 physical items and 9 psychological items. Sum of 20 physical condition items converted into a 0-100 score range, where missing items are imputed by average of total of non-missing items when no more than 50% are missing (otherwise the total score is missing). A lower total score indicates less physically-related impact while a higher total score indicates greater physically-related impact on a participant's functioning. Decreases from

	Baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	256	264	118	31
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	-12.1 (1.12)	-10.3 (1.09)	-8.3 (1.40)	-12.5 (2.58)
Row Title: Month 3	-15.0 (1.16)	-13.3 (1.13)	-10.6 (1.47)	-12.6 (2.72)
Row Title: Month 6	-12.0 (1.22)	-10.9 (1.19)	-8.4 (1.58)	-14.9 (2.94)
Row Title: Month 9	-10.5 (1.27)	-8.9 (1.25)	-7.9 (1.67)	-10.4 (3.13)

Row Title: Month 12	-10.9 (1.27)	-8.2 (1.25)	-6.2 (1.66)	-11.9 (3.15)
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▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects.

		An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures

		with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant

		error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age,

		gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.0009

Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 physical score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS

		score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

16. Secondary Outcome

Title:	Change From Baseline in the MSIS-29 Psychological Score at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	The MSIS-29 is a disease-specific patient-reported outcome measure that has been developed and validated to examine the physical and psychological impact of MS from a patient's perspective; it measures 20 physical items and 9 psychological items. Sum of 9 psychological condition items converted into a 0-100 score range, where missing items are imputed by average of total of non-missing items when no more than 50% are missing (otherwise the total score is missing). A lower total score indicates less psychologically-related impact while a higher total score indicates greater psychologically-related impact on a participant's functioning. Decreases from Baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	257	263	118	31
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	-9.4 (1.09)	-6.5 (1.07)	-8.3 (1.37)	-7.5 (2.53)
Row Title: Month 3	-11.2 (1.17)	-8.9 (1.15)	-9.1 (1.51)	-8.6 (2.80)
Row Title: Month 6	-8.8 (1.23)	-6.8 (1.22)	-8.7 (1.62)	-7.9 (3.06)
Row Title: Month 9	-8.3 (1.29)	-5.1 (1.27)	-8.2 (1.70)	-8.3 (3.21)
Row Title: Month 12	-9.3 (1.29)	-5.3 (1.28)	-7.4 (1.71)	-5.1 (3.29)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects.

		An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures

		with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0032
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant

		error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0021
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type,

		age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0097
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	<0.0001

Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0103
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline

		EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical	Comparison Groups	Primary-Progressive MS
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Analysis Overview	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline MSIS-29 psychological score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1227
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

17. Secondary Outcome

Title:	Change From Baseline in the Activity Limitation Scale (ALS) of PRIMUS Score at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	The PRIMUS activity measure is a 15-item assessment of patient-reported activities of daily living. The total score was calculated as sum of all 15 items converted into a 0-30 range, where missing items were imputed by average of non-missing total when no more than 50% of items were missing (otherwise, the total score is missing). Higher score indicates worse condition. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10

	continued 10 mg fampridine twice daily for 44 weeks.	continued 10 mg fampridine twice daily for 44 weeks.	continued 10 mg fampridine twice daily for 44 weeks.	mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	198	187	87	26
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	-2.5 (0.29)	-1.1 (0.27)	-0.5 (0.39)	-1.7 (0.70)
Row Title: Month 3	-3.2 (0.31)	-2.1 (0.29)	-1.6 (0.42)	-1.9 (0.77)
Row Title: Month 6	-2.3 (0.35)	-1.3 (0.34)	-0.8 (0.48)	-1.6 (0.88)
Row Title: Month 9	-2.4 (0.35)	-0.7 (0.33)	-0.3 (0.48)	-2.0 (0.88)
Row Title: Month 12	-2.0 (0.37)	-0.5 (0.36)	0.7 (0.52)	-1.2 (0.97)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical	Comparison Groups	Secondary-Progressive MS
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Analysis Overview	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1754
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0192
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the

		past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0157
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect

		model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
▼ Statistical Analysis 11 		
Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1012
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0749
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0455
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4699
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline of the total

		ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0235
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1978
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1977
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline of the total ALS score, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2250
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

18. Secondary Outcome

Title:	Change From Baseline in Current Health State of the EQ-5D VAS at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	EQ-5D is a participant-answered questionnaire containing a descriptive system of 5 dimensions - mobility, self-care, usual activities, pain/discomfort and anxiety/depression and a VAS on health state. The EQ-5D VAS ranges from 0 (worst health state) to 100 (best health state). An increase from baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12

Safety Issue? No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	256	258	116	29
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	8.8 (1.06)	6.5 (1.04)	6.7 (1.34)	4.7 (2.53)
Row Title: Month 3	10.1 (1.17)	8.2 (1.15)	7.3 (1.53)	4.6 (2.91)
Row Title: Month 6	8.0 (1.22)	6.1 (1.21)	6.0 (1.63)	4.1 (3.12)
Row Title: Month 9	8.2 (1.25)	5.6 (1.24)	7.9 (1.66)	5.5 (3.22)
Row Title: Month 12	8.8 (1.26)	6.1 (1.26)	5.5 (1.70)	4.5 (3.36)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	<0.0001
	Comments	[Not specified]

Hypothesis		
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0649
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction,

		baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical	Comparison Groups	Progressive-Relapsing MS
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Analysis Overview	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1138
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0003
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1850
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced

		within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect

		model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0887
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
▼ Statistical Analysis 17 		
Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0011
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1853
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

19. Secondary Outcome

Title:	Change From Baseline in EQ-5D Index Scores at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	EQ-5D is a participant-answered questionnaire containing a descriptive system on 5 dimensions - mobility, self-care, usual activities, pain/discomfort and anxiety/depression and a VAS on health state. The scores on the 5 dimensions of descriptive system can be converted into an index score by applying UK weights. EQ-5D index score ranges from 1 to -0.59, and 1 reflects the best outcome. An increase from baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description
Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-	Participants in the Responder group with secondary-	Participants in the Responder group with primary-	Participants in the Responder group with progressive-relapsing MS

	remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	(PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	254	262	114	31
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	0.05 (0.01)	0.04 (0.01)	0.05 (0.02)	0.07 (0.03)
Row Title: Month 3	0.07 (0.01)	0.06 (0.01)	0.05 (0.02)	0.06 (0.03)
Row Title: Month 6	0.04 (0.01)	0.05 (0.01)	0.05 (0.02)	0.09 (0.04)
Row Title: Month 9	0.05 (0.01)	0.02 (0.01)	0.04 (0.02)	0.02 (0.04)
Row Title: Month 12	0.04 (0.01)	0.03 (0.01)	0.05 (0.02)	0.10 (0.04)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0005
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model

		within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0027
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0167
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores,

		MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0024
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.0669

Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0018
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0004
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0190
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction,

		baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0106
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0009
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical	Comparison Groups	Secondary-Progressive MS
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Analysis Overview	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1937
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0445
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6475
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0097
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0386
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced

		within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0219
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline of the current health state of EQ-5D scores, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0076
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

20. Secondary Outcome

Title:	Change From Baseline in Percent Work Time Missed Due to MS on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by MS Disease Type:
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	Responders
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.

	44 weeks.			
Number of Participants Analyzed	93	55	34	9
Least Squares Mean (Standard Error) Unit of measure: percentage of work time missed				
Row Title: Overall	-2.9 (2.01)	-1.5 (2.51)	-2.5 (2.86)	-4.0 (5.82)
Row Title: Month 3	-3.1 (2.49)	-2.6 (3.18)	-3.3 (3.81)	-1.1 (8.51)
Row Title: Month 6	-6.4 (2.23)	-5.3 (2.79)	-3.3 (3.15)	-2.3 (6.29)
Row Title: Month 9	-1.9 (2.86)	2.0 (3.68)	-1.1 (4.44)	-10.0 (8.77)
Row Title: Month 12	-0.3 (2.67)	-0.1 (3.44)	-2.2 (4.12)	-2.7 (8.24)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1471
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage

		of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5503
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3854
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4893
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2166
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4149
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model

		within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3849
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8980
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS,

		MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0046
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0594
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2975
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.7155

Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5070
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5848
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8020
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction,

		baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2540
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9057
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical	Comparison Groups	Secondary-Progressive MS
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Analysis Overview	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9679
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5875
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of work time missed due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7440
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

21. Secondary Outcome

Title:	Change From Baseline in Percent Impairment While Working Due to MS on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The

	'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	106	62	40	9
Least Squares Mean (Standard Error) Unit of measure: percentage of impairment while working				
Row Title: Overall	-5.8 (1.95)	-4.2 (2.43)	0.8 (2.78)	-7.3 (5.95)
Row Title: Month 3	-8.6 (2.28)	-8.0 (2.88)	-1.7 (3.38)	-2.9 (7.57)
Row Title: Month 6	-6.7 (2.20)	-8.7 (2.79)	-2.5 (3.26)	-8.3 (6.88)
Row Title: Month 9	-5.0 (2.49)	-1.8 (3.17)	0.5 (3.85)	-4.9 (8.51)
Row Title: Month 12	-2.9 (2.56)	1.4 (3.35)	6.8 (3.95)	-13.1 (8.38)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0032
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0828
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7756
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses

		experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2200
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical	Comparison Groups	Secondary-Progressive MS
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Analysis Overview	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0061
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.6258

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6987
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was

		used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0025
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0021
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures

		with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4385
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2275
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0446
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5757
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8936
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type

		interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5675
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2539
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6673
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0849
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of impairment while working due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1187
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

22. Secondary Outcome

Title:	Change From Baseline in Percent Overall Work Impairment Due to MS on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to

	100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	92	52	33	9
Least Squares Mean (Standard Error) Unit of measure: percentage of overall work impairment				
Row Title: Overall	-7.5 (2.41)	-6.8 (3.09)	-0.8 (3.54)	-6.5 (6.97)

Row Title: Month 3	-10.7 (2.74)	-10.4 (3.56)	-1.7 (4.18)	2.9 (9.51)
Row Title: Month 6	-9.2 (2.81)	-11.9 (3.60)	-3.3 (4.22)	-6.5 (8.10)
Row Title: Month 9	-4.9 (3.49)	-2.6 (4.61)	1.2 (5.62)	-9.7 (11.15)
Row Title: Month 12	-5.3 (2.84)	-2.1 (3.73)	0.4 (4.42)	-12.6 (8.31)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0022
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was

		used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0299
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8135
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures

		with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3526
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0039
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6924
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7639
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type

		interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0013
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0011
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4340
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4224
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1628
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An

		unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5666
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8315
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect

		model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3852
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0652
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5719
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9237
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of overall work impairment due to MS, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1310
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

23. Secondary Outcome

Title:	Change From Baseline in Regular Activity Productivity Loss on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by MS Disease Type: Responders
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at

	work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Relapsing-Remitting MS	Secondary-Progressive MS	Primary-Progressive MS	Progressive-Relapsing MS
▼ Arm/Group Description:	Participants in the Responder group with relapsing-remitting MS (RRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with secondary-progressive MS (SPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with primary-progressive MS (PPMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants in the Responder group with progressive-relapsing MS (PRMS). Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.
Number of Participants Analyzed	251	252	116	31

Least Squares Mean (Standard Error) Unit of measure: percentage of activity impairment				
Row Title: Overall	-14.9 (1.49)	-9.8 (1.47)	-7.1 (1.86)	-12.2 (3.39)
Row Title: Month 3	-16.2 (1.74)	-13.4 (1.72)	-8.7 (2.29)	-11.0 (4.28)
Row Title: Month 6	-15.1 (1.76)	-11.1 (1.76)	-9.0 (2.35)	-14.2 (4.35)
Row Title: Month 9	-14.9 (1.79)	-7.5 (1.78)	-7.1 (2.35)	-10.8 (4.46)
Row Title: Month 12	-13.5 (1.79)	-7.1 (1.79)	-3.7 (2.37)	-13.0 (4.51)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Overall, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Overall, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type

		interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Overall, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Overall, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0003
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 3, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 3, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 3, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An

		unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 3, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0102
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 6, RRMS. Mixed effect

		model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 6, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 6, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 6, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0012
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 9, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender,

		country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 9, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0026
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 9, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0161
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Relapsing-Remitting MS
	Comments	Month 12, RRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Secondary-Progressive MS
	Comments	Month 12, SPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Primary-Progressive MS
	Comments	Month 12, PPMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses

		experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1151
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Progressive-Relapsing MS
	Comments	Month 12, PRMS. Mixed effect model for repeated measures with visit, baseline of percentage of regular activity productivity loss, MS type, age, gender, country, visit and MS type interaction, baseline EDSS score and total number of relapses experienced within the past 12 months as fixed effects. An unstructured covariance was used to model within-participant error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0040
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Title:	Change From Baseline in the PCS of the SF-36 at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	The SF-36 determines participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 primarily contribute to the PCS score of the SF-36. Items 5-8 primarily contribute to the MCS score of the SF-36. Scores on each item are summed and averaged (range: 0=worst to 100=best). Increases from baseline indicate improvement. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	521	58	145	23

Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	3.1 (0.36)	-0.3 (0.71)	3.9 (0.48)	-0.6 (1.08)
Row Title: Month 3	4.0 (0.38)	0.1 (0.77)	4.1 (0.53)	-1.2 (1.19)
Row Title: Month 6	3.1 (0.40)	0.6 (0.89)	3.9 (0.58)	-0.8 (1.35)
Row Title: Month 9	2.7 (0.40)	-1.2 (0.91)	4.0 (0.58)	-0.7 (1.46)
Row Title: Month 12	2.5 (0.40)	-0.8 (0.94)	3.6 (0.58)	0.2 (1.44)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6769
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5780
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced

		as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	3.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.68
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	4.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.10
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis	Comparison Groups	Non-responder: Taking Additional MS Therapy
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Overview	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8886
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3221
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the

		2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	3.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.75
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	5.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.23
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4668
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5695
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking

		Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0058
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	2.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.88
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total

		number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0010
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	4.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.40
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	<0.0001

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2040
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total

		number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6306
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23

Statistical	Comparison Groups	Responder: Taking Additional MS
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Analysis Overview		Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non- responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	3.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.90
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0020
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	4.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.51
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4052
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the

		2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8626
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0004
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	3.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.93
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy)

		versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline PCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0263
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	3.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.49
	Estimation Comments	[Not specified]

25. Secondary Outcome

Title:	Change From Baseline in the MCS of the SF-36 at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	The SF-36 determines participants' overall quality of life by assessing 1) limitations in physical functioning due to health problems; 2) limitations in usual role because of physical health problems; 3) bodily pain; 4) general health perceptions; 5) vitality; 6) limitations in social functioning because of physical or emotional problems; 7) limitations in usual role due to emotional problems; and 8) general mental health. Items 1-4 primarily contribute to the PCS score of the SF-36. Items 5-8 primarily contribute to the MCS score of the SF-36. Scores on each item are summed and averaged (range: 0=worst to 100=best). Increases from baseline indicate improvement. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).

Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	522	58	145	23
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	2.8 (0.56)	-0.1 (1.09)	3.9 (0.74)	0.6 (1.64)
Row Title: Month 3	4.0 (0.59)	-1.3 (1.18)	4.8 (0.81)	1.1 (1.82)
Row Title: Month 6	3.0 (0.60)	0.2 (1.29)	4.1 (0.85)	1.5 (1.96)
Row Title: Month 9	2.1 (0.62)	1.3 (1.40)	2.8 (0.89)	0.0 (2.24)
Row Title: Month 12	2.1 (0.61)	-0.7 (1.40)	3.9 (0.87)	-0.3 (2.15)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8999
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS

		score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7156
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0050
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	2.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.03
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0490
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	3.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.68

	Estimation Comments	[Not specified]
▼ Statistical Analysis 7 		
Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2740
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy):

		Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5556
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	5.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.15
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0476
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of	Estimation Parameter	Other[difference of LS means]

Estimation	Estimated Value	3.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.88
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country,

		baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8627
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

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Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4312
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0305
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	2.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.27
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2059
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	2.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.03
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0008
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated

		measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3685
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0016
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 22

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9862
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total

		number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5561
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.38
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2281
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	2.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.32
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0006
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical	Comparison Groups	Non-responder: Taking Additional MS
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Analysis Overview		Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6004
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9040
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the

		2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0401
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	2.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.38
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the 2-way and 3-way interactions among them, baseline MCS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0651
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	4.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.23
	Estimation Comments	[Not specified]

26. Secondary Outcome

Title:	Change From Baseline in the MSIS-29 Physical Score at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	The MSIS-29 is a disease specific patient-reported outcome measure that has been developed and validated to examine the physical and psychological impact of MS from a patient's perspective; it measures 20 physical items and 9 psychological items. Sum of 20 physical condition items converted into a 0-100 score range, where missing items are imputed by average of total of non-missing items when no more than 50% are missing (otherwise the total score is missing). A lower total score indicates less physically-related impact while a higher total score indicates greater physically-related impact on a participant's functioning. Decreases from Baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	524	57	145	22
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	-9.6 (1.05)	-1.5 (2.03)	-12.2 (1.38)	-3.2 (3.10)
Row Title: Month 3	-12.6 (1.07)	-1.4 (2.08)	-14.0 (1.43)	-4.0 (3.22)
Row Title: Month 6	-10.0 (1.10)	-2.2 (2.28)	-12.2 (1.52)	-5.2 (3.47)
Row Title: Month 9	-8.0 (1.13)	-0.4 (2.48)	-11.8 (1.61)	0.5 (4.02)
Row Title: Month 12	-7.8 (1.13)	-2.1 (2.57)	-11.1 (1.61)	-4.3 (3.95)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country,

		baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4540
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2949
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-8.1
	Parameter Dispersion	Type: Standard Error of the mean

		Value: 1.93
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0046
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-9.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.16
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis	Comparison Groups	Responder: Taking Additional MS Therapy
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Overview	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-12.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.07
	Estimation Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total

		number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5020
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

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Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2157
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model

		within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-11.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.00
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0026
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-10.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.30
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical	Comparison Groups	Non-responder: Taking Additional MS
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Analysis Overview		Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3435
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1357
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed

		effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0004
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-7.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.22
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country,

		baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0511
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-7.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.58
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8703
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them,

		baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9049
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0019
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-7.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.44
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking

		Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0033
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-12.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.15
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country,

		baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4087
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2755
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0251
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-5.7
	Parameter Dispersion	Type: Standard Error of the mean

		Value: 2.52
	Estimation Comments	[Not specified]
▼ Statistical Analysis 30 		
Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 physical score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0989
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-6.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.08
	Estimation Comments	[Not specified]

27. Secondary Outcome

Title:	Change From Baseline in MSIS-29 Psychological Score at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	The MSIS-29 is a disease-specific patient-reported outcome measure that has been developed and validated to examine the physical and psychological impact of MS from a patient's perspective; it measures 20 physical items and 9 psychological items. Sum of 9 psychological condition items converted into a 0-100 score range, where missing items are imputed by average of total of non-missing items when no more than 50% are missing (otherwise the total score is missing). A lower total score indicates less psychologically-related impact while a higher total score indicates greater psychologically-related impact on a participant's functioning. Decreases from Baseline indicate improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.

	weeks.		weeks.	
Number of Participants Analyzed	525	57	144	22
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	-7.1 (1.02)	-0.3 (2.00)	-9.7 (1.36)	-2.8 (3.06)
Row Title: Month 3	-9.0 (1.07)	0.2 (2.17)	-11.1 (1.49)	-1.0 (3.39)
Row Title: Month 6	-7.1 (1.10)	-2.6 (2.37)	-9.5 (1.56)	-2.6 (3.60)
Row Title: Month 9	-6.1 (1.13)	-0.2 (2.57)	-8.9 (1.64)	-2.4 (4.22)
Row Title: Month 12	-6.2 (1.13)	1.3 (2.70)	-9.1 (1.67)	-5.1 (4.16)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis	Comparison Groups	Non-responder: Taking Additional MS Therapy
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Overview	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8767
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3673
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated

		measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0004
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-6.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.91
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total

		number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0273
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-6.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.12
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9091
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them,

		baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7718
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-9.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.11
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking

		Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0038
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-10.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.50
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country,

		baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2720
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4767
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0553
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-4.5
	Parameter Dispersion	Type: Standard Error of the mean

		Value: 2.32
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0632
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-6.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.73
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis	Comparison Groups	Responder: Taking Additional MS Therapy
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Overview	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20 

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9398
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Not

		Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5655
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0204
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-5.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.54
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.1414

Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-6.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.37
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy

	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6279
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2239
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated

		measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0049
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-7.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.67
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline MSIS-29 psychological score, age, gender, country, baseline EDSS score and total

		number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3457
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-4.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.32
	Estimation Comments	[Not specified]

28. Secondary Outcome

Title:	Change From Baseline in the Activities Limitation Scale of the PRIMUS at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	The PRIMUS activity measure is a 15-item assessment of patient-reported activities of daily living. The total score was calculated as sum of all 15 items converted into a 0-30 range, where missing items were imputed by average of non-missing total when no more than 50% of items were missing (otherwise, the total score is missing). Higher score indicates worse condition. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	395	33	103	12
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	-1.3 (0.24)	0.8 (0.63)	-1.9 (0.37)	0.8 (1.11)
Row Title: Month 3	-2.1 (0.25)	-0.5 (0.67)	-2.9 (0.40)	-0.0 (1.14)
Row Title: Month 6	-1.2 (0.27)	0.6 (0.81)	-2.1 (0.46)	1.3 (1.33)
Row Title: Month 9	-1.1 (0.27)	2.0 (0.82)	-1.6 (0.46)	1.1 (1.67)
Row Title: Month 12	-0.7 (0.29)	1.1 (0.93)	-1.0 (0.50)	1.0 (1.81)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them,

		baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2087
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model

		within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4487
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0013
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of	Estimation Parameter	Other[difference of LS means]

Estimation	Estimated Value	-2.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.64
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0188
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-2.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.15
	Estimation Comments	[Not specified]

Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4243
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not

		Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9989
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0207
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-1.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.68
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0161
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-2.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.18
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4256
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]

	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3313
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them,

		baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0238
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-1.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.83
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0150
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-3.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.39
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0171
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0007
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5146
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23

Statistical Analysis	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking
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Overview		Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0003
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-3.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.84
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1224
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-2.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.72
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0168
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2272
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy):

		Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0570
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.5832

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0561
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-1.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.94
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the total ALS score, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2971
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-1.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.86
	Estimation Comments	[Not specified]

29. Secondary Outcome

Title:	Change From Baseline in the Current Health State of EQ-5D VAS at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	EQ-5D is a participant-answered questionnaire containing a descriptive system of 5 dimensions - mobility, self-care, usual activities, pain/discomfort and anxiety/depression and a VAS on health state. The EQ-5D VAS ranges

	from 0 (worst health state) to 100 (best health state). An increase from baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	518	58	141	21
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	6.0 (1.00)	-5.8 (1.95)	8.6 (1.33)	-0.8 (3.04)
Row Title: Month 3	7.6 (1.06)	-3.9 (2.16)	8.6 (1.49)	-1.2 (3.46)
Row Title: Month 6	5.2 (1.09)	-5.6 (2.35)	8.6 (1.56)	1.5 (3.72)
Row Title: Month 9	5.5 (1.11)	-6.1 (2.51)	8.7 (1.62)	-1.8 (4.13)

Row Title: Month 12	5.5 (1.12)	-7.7 (2.67)	8.7 (1.67)	-1.5 (4.33)
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▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS

		score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0029
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8041
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS

		score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	11.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 1.85
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority	No

	or Equivalence Analysis?	
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0026
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	9.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.10
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]

	Comments	[Not specified]
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▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0689
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of

		relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.7182
	Comments	[Not specified]
	Method	Other [mixed effect model]
Statistical Test of Hypothesis	Comments	[Not specified]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	11.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.10
	Estimation Comments	[Not specified]
▼ Statistical Analysis 12 		
Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus

		Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0061
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	9.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.57
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age,

		gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0179
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed

		effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6911
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	10.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.31
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0666
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	7.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.85

	Estimation Comments	[Not specified]
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▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of

		relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0158
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6684
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of

		relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	11.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.49
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0141
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	10.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.28
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0042
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7329
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical	Comparison Groups	Responder: Taking Additional MS
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Analysis Overview		Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	13.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.65
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy):

		Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0242
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	10.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.49
	Estimation Comments	[Not specified]

30. Secondary Outcome

Title:	Change From Baseline in the Index Scores of EQ-5D at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	EQ-5D is a participant-answered questionnaire containing a descriptive system on 5 dimensions - mobility, self-care, usual activities, pain/discomfort and anxiety/depression and a VAS on health state. The scores on the 5 dimensions of descriptive system can be converted into an index score by applying UK weights. EQ-5D index score ranges from 1 to -0.59, and 1 reflects the best outcome. An increase from baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The 'overall' estimate is the average change from baseline over the whole time period (through Month 12).

Time Frame:	Baseline, Months 3, 6, 9, 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	519	56	142	22
Least Squares Mean (Standard Error) Unit of measure: units on a scale				
Row Title: Overall	0.04 (0.01)	-0.00 (0.02)	0.06 (0.02)	0.02 (0.03)
Row Title: Month 3	0.07 (0.01)	0.02 (0.02)	0.07 (0.02)	-0.02 (0.04)
Row Title: Month 6	0.05 (0.01)	-0.00 (0.03)	0.05 (0.02)	0.03 (0.04)
Row Title: Month 9	0.03 (0.01)	-0.00 (0.03)	0.06 (0.02)	0.02 (0.05)
Row Title: Month 12	0.03 (0.01)	-0.03 (0.03)	0.07 (0.02)	0.04 (0.05)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9151
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Non-responder (Not

		Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6128
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0331
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.05
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.02
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.1919

Test of Hypothesis	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.05
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.04
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical	Comparison Groups	Non-responder: Taking Additional MS
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Analysis Overview	Therapy	
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4481
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5454
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy

	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0516
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.05
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.02
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0175
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.09
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.04
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9371
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical	Comparison Groups	Responder: Not Taking Additional MS
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Analysis Overview		Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0056
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5475
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.0699
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]

	Estimated Value	0.05
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.03
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5870
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.02
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.05
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0245
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9926
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0027
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6368
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23 

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3358
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.03
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.03
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5089
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.03
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.05
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.0141
	Comments	[Not specified]
	Method	Other [mixed effect model]
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.0141
	Comments	[Not specified]
	Method	Other [mixed effect model]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4280
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0002
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.3827
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0748
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.06
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.03
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the current health state of EQ-5D index scores, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5663
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[least squares mean]
	Estimated Value	0.03
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.05
	Estimation Comments	[Not specified]

31. Secondary Outcome

Title:	Change From Baseline in Percent Work Time Missed Due to MS on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The

	'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	149	12	42	2
Least Squares Mean (Standard Error) Unit of measure: percentage of work time missed				
Row Title: Overall	-3.0 (2.10)	-11.9 (4.93)	-2.4 (2.72)	14.9 (12.11)
Row Title: Month 3	-3.7 (2.43)	-8.3 (6.14)	-2.0 (3.43)	28.6 (17.71)
Row Title: Month 6	-6.0 (2.21)	-10.3 (5.52)	-4.3 (2.98)	6.4 (12.11)
Row Title: Month 9	-1.2 (2.60)	-12.8 (8.32)	-2.1 (4.09)	13.9 (21.98)
Row Title: Month 12	-1.0 (2.53)	-16.2 (7.16)	-1.1 (3.79)	10.6 (15.59)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1544
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0167
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3868
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2214
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0743
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	8.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.96
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1601
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-17.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 12.22
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1251
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1764
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5528
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.1080
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4644
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	4.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.27
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0887
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-30.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 17.91
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0071
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0640
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical	Comparison Groups	Responder: Not Taking Additional MS
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Analysis Overview	Therapy	
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1552
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5979
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.4444
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]

	Estimated Value	4.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.58
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3863
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-10.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 12.27
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6352
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1265
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6161
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5280
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23 

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1769
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	11.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 8.51
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4743
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-16.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 22.24
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6901
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0245
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7707
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.4989
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0387
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	15.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.31
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % work time missed due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4635
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-11.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 15.88
	Estimation Comments	[Not specified]

32. Secondary Outcome

Title:	Change From Baseline in Percent Impairment While Working Due to MS on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The

	'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	168	13	49	3
Least Squares Mean (Standard Error) Unit of measure: percentage of impairment while working				
Row Title: Overall	-3.1 (2.10)	-7.3 (5.00)	-6.4 (2.69)	-11.5 (10.86)
Row Title: Month 3	-6.1 (2.35)	-1.0 (6.02)	-8.1 (3.24)	-3.3 (14.07)
Row Title: Month 6	-5.6 (2.26)	-3.8 (5.89)	-8.0 (3.06)	-15.9 (13.27)
Row Title: Month 9	-1.9 (2.44)	-19.0 (7.31)	-5.6 (3.55)	-6.0 (18.93)
Row Title: Month 12	1.1 (2.49)	-5.5 (7.56)	-3.8 (3.65)	-20.7 (15.27)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1392
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1448
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0187
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2920
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3968
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	4.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.95
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6420
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	5.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 10.95
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0100
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8634
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0134
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.8147
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4035
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-5.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.06
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7385
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-4.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 14.25
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0139
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5207
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical	Comparison Groups	Responder: Not Taking Additional MS
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Analysis Overview		Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0091
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2312
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.7578
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]

	Estimated Value	-1.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.89
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5575
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	7.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 13.42
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4486
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0102
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1185
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7523
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23 

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0214
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	17.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.38
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9826
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 19.12
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6627
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4674
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2965
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.1778
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3903
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	6.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.65
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % impairment while working due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2794
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	16.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 15.53
	Estimation Comments	[Not specified]

33. Secondary Outcome

Title:	Change From Baseline in Percent Overall Work Impairment Due to MS on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The

	'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	145	11	41	2
Least Squares Mean (Standard Error) Unit of measure: percentage of overall work impairment				
Row Title: Overall	-4.8 (2.55)	-9.9 (6.26)	-6.7 (3.32)	1.2 (14.53)
Row Title: Month 3	-7.9 (2.84)	-6.6 (6.99)	-7.1 (3.85)	18.0 (21.17)
Row Title: Month 6	-7.8 (2.78)	-1.8 (7.48)	-7.7 (3.85)	-8.2 (15.87)
Row Title: Month 9	-1.6 (3.22)	-18.5 (10.69)	-5.5 (5.15)	3.7 (25.71)
Row Title: Month 12	-1.8 (2.81)	-12.6 (7.95)	-6.5 (4.02)	-8.6 (15.29)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0628
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1166
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0451
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9327
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4177
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	5.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.28
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5885
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-7.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 14.64
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0059
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3467
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0654
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.3965
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8548
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-1.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.11
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2405
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-25.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 21.35
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0056
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8105
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical	Comparison Groups	Responder: Not Taking Additional MS
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Analysis Overview		Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0470
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6067
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.4309
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]

	Estimated Value	-6.0
	Parameter Dispersion	Type: Standard Error of the mean Value: 7.56
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9761
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 16.09
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.6261
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0860
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2884
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8854
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23 

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured

		covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1226
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	16.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 10.88
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.7249
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-9.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 26.07
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.5129
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1138
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1086
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.5746
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1831
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	10.8
	Parameter Dispersion	Type: Standard Error of the mean Value: 8.07
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the % overall work impairment due to MS, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.8917
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	2.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 15.54
	Estimation Comments	[Not specified]

34. Secondary Outcome

Title:	Change From Baseline in Regular Activity Productivity Loss on the WPAI-SHP Questionnaire at Months 3, 6, 9, and 12 by Whether Taking Additional MS Therapy
▼ Description:	WPAI-SHP is a 6-question participant-rated questionnaire to determine degree to which a specific health problem affected work productivity while at work and outside of work. Four scores are derived: percentage of absenteeism (percentage of work time missed) and presenteeism (reduced productivity while at work), overall work impairment score combining absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Score range: 0 (not affected/no impairment) to 100 (completely affected/impaired). WPAI outcomes are expressed as impairment percentages with higher numbers indicating greater impairment and less productivity. A decrease from Baseline indicates improvement. A mixed effect model for repeated measures was used for this analysis. An unstructured covariance was used to model within-participant error. The

	'overall' estimate is the average change from baseline over the whole time period (through Month 12).
Time Frame:	Baseline, Months 3, 6, 9, and 12
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

Participants in the intent-to-treat population (all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit) who were included in the mixed effect model for repeated measures analysis.

Arm/Group Title	Responder: Taking Additional MS Therapy	Non-responder: Taking Additional MS Therapy	Responder: Not Taking Additional MS Therapy	Non-responder: Not Taking Additional MS Therapy
▼ Arm/Group Description:	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants (not taking additional MS therapy) took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	509	56	141	21
Least Squares Mean (Standard Error) Unit of measure: percentage of activity impairment				
Row Title: Overall	-10.6 (1.39)	-4.2 (2.69)	-13.3 (1.83)	-3.1 (4.15)
Row Title: Month 3	-12.7 (1.53)	-3.4 (3.24)	-15.7 (2.20)	-1.8 (5.15)
Row Title: Month 6	-11.5 (1.54)	-6.3 (3.40)	-14.6 (2.23)	-0.5 (5.20)
Row Title: Month 9	-9.8 (1.55)	-5.9 (3.50)	-12.0 (2.28)	1.6 (5.86)
Row Title: Month 12	-8.5 (1.56)	-1.3 (3.70)	-10.9 (2.31)	-11.6 (5.72)

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Overall, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1152
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 3

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 4

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Overall, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.4578
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 5

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Overall, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0125
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-6.4
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.56
	Estimation Comments	[Not specified]

▼ Statistical Analysis 6

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Overall, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0158
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-10.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.23
	Estimation Comments	[Not specified]

▼ Statistical Analysis 7

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 3, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 8

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2894
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 9

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 10

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.7230
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 11

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 3, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0038
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-9.3
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.20
	Estimation Comments	[Not specified]

▼ Statistical Analysis 12

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 3, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0097
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-13.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.37
	Estimation Comments	[Not specified]

▼ Statistical Analysis 13

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 14

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0628
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 15

Statistical	Comparison Groups	Responder: Not Taking Additional MS
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Analysis Overview		Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 16

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9232
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 17

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 6, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.1249
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]

	Estimated Value	-5.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.37
	Estimation Comments	[Not specified]

▼ Statistical Analysis 18

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 6, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0093
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-14.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.42
	Estimation Comments	[Not specified]

▼ Statistical Analysis 19

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 20

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0937
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 21

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 22

Statistical	Comparison Groups	Non-responder: Not Taking
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Analysis Overview		Additional MS Therapy
	Comments	Month 9, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7814
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 23 

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
	Comments	Month 9, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was

		used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2561
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-3.9
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.47
	Estimation Comments	[Not specified]

▼ Statistical Analysis 24

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 9, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0255
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-13.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.07
	Estimation Comments	[Not specified]

▼ Statistical Analysis 25

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy
	Comments	Month 12, Responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 26

Statistical Analysis Overview	Comparison Groups	Non-responder: Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.7241
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 27

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 28

Statistical Analysis Overview	Comparison Groups	Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
Statistical Test of Hypothesis	Comments	[Not specified]
	P-Value	0.0427
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]

▼ Statistical Analysis 29

Statistical Analysis Overview	Comparison Groups	Responder: Taking Additional MS Therapy, Non-responder: Taking Additional MS Therapy
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	Comments	Month 12, Responder (Taking Additional MS Therapy) versus Non-responder (Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0498
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	-7.2
	Parameter Dispersion	Type: Standard Error of the mean Value: 3.67
	Estimation Comments	[Not specified]

▼ Statistical Analysis 30

Statistical Analysis Overview	Comparison Groups	Responder: Not Taking Additional MS Therapy, Non-responder: Not Taking Additional MS Therapy
	Comments	Month 12, Responder (Not Taking Additional MS Therapy) versus Non-responder (Not Taking Additional MS Therapy): Mixed effect model for repeated measures with visit, responder

		group, additional MS therapy, the two-way and three-way interactions among them, baseline of the regular activity productivity loss, age, gender, country, baseline EDSS score and total number of relapses experienced as fixed effects. An unstructured covariance was used to model within-patient error.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.9078
	Comments	[Not specified]
	Method	Other [mixed effect model]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[difference of LS means]
	Estimated Value	0.7
	Parameter Dispersion	Type: Standard Error of the mean Value: 5.95
	Estimation Comments	[Not specified]

35. Secondary Outcome

Title:	Number of Participants With Adverse Events (AEs) and Serious AEs (SAEs)
▼ Description:	AE: any untoward medical occurrence that did not necessarily have a causal relationship with study treatment. SAE: any untoward medical occurrence that at any dose: resulted in death; in the view of the Investigator, placed the subject at immediate risk of death (a life threatening event); required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; resulted in a congenital anomaly/birth defect; any other medically important event that, in the opinion of the Investigator, could have jeopardized the subject or may have required intervention to prevent one of the other outcomes listed in the definition above.
Time Frame:	From signing of Informed Consent (SAEs) or from first dose of study treatment (AEs) through Week 50 or Early Termination (14 +/- 7 days after last dose)

Safety Issue? No

▼ Outcome Measure Data 

▼ Analysis Population Description

Intent-to-treat population: all participants who received at least 1 dose of study treatment and who provided at least 1 efficacy assessment at Baseline and the 3-month visit.

Arm/Group Title	Responder	Non-responder	All Participants
▼ Arm/Group Description:	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	All participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
Number of Participants Analyzed	707	128	835
Measure Type: Number Unit of measure: participants			
Row Title: AE	522	64	586
Row Title: SAE	76	3	79
Row Title: Severe AE	48	2	50
Row Title: Study treatment related AE	248	37	285
Row Title: Study treatment related SAE	7	0	7
Row Title: Death	2	0	2
Row Title: AE leading to study drug discontinuation	32	8	40
Row Title: AE leading to study discontinuation	18	1	19

 Adverse Events

Time Frame	From signing of Informed Consent (SAEs) or from first dose of study treatment (AEs) through Week 50 or Early Termination (14 +/- 7 days after last dose).		
Additional Description			
Source Vocabulary Name	MedDRA 16.0		
Assessment Type	Systematic Assessment		
Arm/Group Title ▼ Arm/Group Description	Responder	Non-responder	All Participants
	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks.	Participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.	All participants took 10 mg fampridine twice daily for the first 4 weeks. Those deemed treatment responders continued 10 mg fampridine twice daily for 44 weeks. Those deemed treatment non-responders continued without treatment by completing quality of life questionnaires.
▼ Serious Adverse Events			
	Responder	Non-responder	All Participants
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	76/707 (10.75%)	3/128 (2.34%)	79/835 (9.46%)
Blood and lymphatic system disorders			
Anaemia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Microcytic Anaemia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Cardiac disorders			
Arrhythmia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Atrial Fibrillation † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Cardiovascular Disorder † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Myocardial Infarction † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Gastrointestinal disorders			
Colitis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
General disorders			

Death † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Hepatobiliary disorders			
Cholecystitis Acute † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Infections and infestations			
Appendicitis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Chronic Sinusitis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Gastrointestinal Viral Infection † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Peritonitis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Pneumonia Influenzal † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Urinary Tract Infection † A	3/707 (0.42%)	1/128 (0.78%)	4/835 (0.48%)
Urosepsis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Viral Infection † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Injury, poisoning and procedural complications			
Avulsion Fracture † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Fall † A	9/707 (1.27%)	0/128 (0%)	9/835 (1.08%)
Fibula Fracture † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Hand Fracture † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Hip Fracture † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Joint Injury † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Lower Limb Fracture † A	0/707 (0%)	1/128 (0.78%)	1/835 (0.12%)
Traumatic Intracranial Haemorrhage † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Upper Limb Fracture † A	2/707 (0.28%)	0/128 (0%)	2/835 (0.24%)
Wound † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Wrist Fracture † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Metabolism and nutrition disorders			
Fluid Retention † A	0/707 (0%)	1/128 (0.78%)	1/835 (0.12%)
Musculoskeletal and connective tissue disorders			

Bursitis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Cervical Spinal Stenosis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Exostosis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Foot Deformity † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Musculoskeletal Pain † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Musculoskeletal Stiffness † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Rotator Cuff Syndrome † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Synovial Cyst † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Vertebral Foraminal Stenosis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Melanoma Stage IV † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Uterine Leiomyoma † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Nervous system disorders			
Cerebral Venous Thrombosis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Cerebrovascular Accident † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Convulsion † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Dyskinesia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Epilepsy † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Grand Mal Convulsion † A	2/707 (0.28%)	0/128 (0%)	2/835 (0.24%)
Multiple Sclerosis † A	2/707 (0.28%)	0/128 (0%)	2/835 (0.24%)
Multiple Sclerosis Relapse † A	19/707 (2.69%)	0/128 (0%)	19/835 (2.28%)
Muscle Spasticity † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Paraesthesia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Paraparesis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Progressive Multiple Sclerosis † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
† A			

Syncope	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Trigeminal Neuralgia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Uhthoff's Phenomenon † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Psychiatric disorders			
Hypomania † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Suicide Attempt † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Renal and urinary disorders			
Bladder Disorder † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Bladder Dysfunction † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Erectile Dysfunction † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Metrorrhagia † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Ovarian Cyst Ruptured † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Respiratory, thoracic and mediastinal disorders			
Lung Disorder † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Skin and subcutaneous tissue disorders			
Decubitus Ulcer † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Surgical and medical procedures			
Liposuction † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Stent Placement † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
Stent Removal † A	1/707 (0.14%)	0/128 (0%)	1/835 (0.12%)
† Indicates events were collected by systematic assessment. A Term from vocabulary, MedDRA 16.0			
▼ Other (Not Including Serious) Adverse Events			
Frequency Threshold for Reporting Other Adverse Events	5%		

	Responder	Non-responder	All Participants
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	314/707 (44.41%)	41/128 (32.03%)	355/835 (42.51%)
Gastrointestinal disorders			
Nausea † A	60/707 (8.49%)	6/128 (4.69%)	66/835 (7.9%)
General disorders			
Fatigue † A	31/707 (4.38%)	7/128 (5.47%)	38/835 (4.55%)
Infections and infestations			
Nasopharyngitis † A	60/707 (8.49%)	1/128 (0.78%)	61/835 (7.31%)
Urinary Tract Infection † A	58/707 (8.2%)	7/128 (5.47%)	65/835 (7.78%)
Injury, poisoning and procedural complications			
Fall † A	50/707 (7.07%)	5/128 (3.91%)	55/835 (6.59%)
Nervous system disorders			
Dizziness † A	35/707 (4.95%)	8/128 (6.25%)	43/835 (5.15%)
Headache † A	74/707 (10.47%)	6/128 (4.69%)	80/835 (9.58%)
Multiple Sclerosis Relapse † A	63/707 (8.91%)	2/128 (1.56%)	65/835 (7.78%)
Psychiatric disorders			
Insomnia † A	83/707 (11.74%)	12/128 (9.38%)	95/835 (11.38%)
† Indicates events were collected by systematic assessment. A Term from vocabulary, MedDRA 16.0			

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

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

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

Our agreement is subject to confidentiality but generally the PI can publish, for noncommercial purposes only, results and methods of the trial, but no other Sponsor Confidential Information. PI must give Sponsor no less than 60 days to review any manuscript for a proposed publication and must delay publication for up to an additional

90 days thereafter if Sponsor needs to file any patent application to protect any of Sponsor's intellectual property contained in the proposed publication.

Results Point of Contact

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