A Prospective, Open-label, Non-randomized, Clinical Trial to Determine if Natalizumab (Tysabri®) Improves Ambulatory Measures in Relapsing-remitting Multiple Sclerosis (RRMS) Patients (TIMER)

This study has been completed.

Sponsor:
Biogen Idec

Collaborator:
Elan Pharmaceuticals

Information provided by (Responsible Party):
Biogen Idec

ClinicalTrials.gov Identifier:
NCT00871780

First received: March 26, 2009
Last updated: November 11, 2014
Last verified: November 2014
History of Changes

Results First Received: November 11, 2014

Study Type:	Interventional
Study Design:	Endpoint Classification: Efficacy Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Relapsing Remitting Multiple Sclerosis (RRMS)
Intervention:	Drug: BG00002 (natalizumab)

Participant Flow

Hide Participant Flow

Recruitment Details

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

Pre-Assignment Details

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

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Participant Flow: Overall Study

	Natalizumab
STARTED	224 [1]
Safety Analysis Population	218 [2]
Efficacy Analysis Population	215 [3]

COMPLETED	197
NOT COMPLETED	27
Enrolled But Not Treated	6
Withdrawal by Subject	9
Adverse Event	6
Voluntary Discontinuation	4
Death	1
Physician Decision	1

[1] number enrolled
[2] participants who had ≥1 infusion of natalizumab during the study
[3] participants who had ≥1 infusion of natalizumab and completed at least 1 on-treatment evaluation

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation)

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Baseline Measures

	Natalizumab
Number of Participants [units: participants]	215
Age [units: years] Mean ± Standard Deviation	35.1 ± 9.56
Gender [units: participants]	
Female	137
Male	78

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline in the Timed 100-meter Walk Test (T100T) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Primary
Measure Title	Change From Baseline in the Timed 100-meter Walk Test (T100T)
Measure Description	In the T100T, the participant is instructed to walk as fast as possible for a distance of 100 meters.

Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Change From Baseline in the Timed 100-meter Walk Test (T100T) [units: seconds] Median (Inter-Quartile Range)	
Baseline; n=215	86.0 (63.7 to 128.9)
Change from Baseline at Week 24; n=207	-1.2 (-11.6 to 1.9)
Change from Baseline at Week 48; n=199	-1.6 (-13.7 to 2.8)

Statistical Analysis 1 for Change From Baseline in the Timed 100-meter Walk Test (T100T)

Groups [1]	Natalizumab
Method [2]	Wilcoxon signed rank test
P Value [3]	0.0003

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Change From Baseline in the Timed 100-meter Walk Test (T100T)

Groups [1]	Natalizumab
Method [2]	Wilcoxon signed rank test

P Value [3]	0.0002

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

2. Primary: Change From Baseline in the Timed 25-foot Walk Test (T25FW) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Primary
Measure Title	Change From Baseline in the Timed 25-foot Walk Test (T25FW)
Measure Description	In the T25FW, the participant is instructed to walk as fast as possible for a distance of 25 feet.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Change From Baseline in the Timed 25-foot Walk Test (T25FW) [units: seconds] Median (Inter-Quartile Range)	
Baseline; n=215	6.6 (5.2 to 10.2)
Change from Baseline at Week 24; n=207	-0.1 (-0.7 to 0.2)
Change from Baseline at Week 48; n=199	-0.1 (-0.6 to 0.3)

Statistical Analysis 1 for Change From Baseline in the Timed 25-foot Walk Test (T25FW)

Groups [1]	Natalizumab

Method [2]	Wilcoxon signed rank test
P Value [3]	0.0148

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Change From Baseline in the Timed 25-foot Walk Test (T25FW)

Groups [1]	Natalizumab
Method [2]	Wilcoxon signed rank test
P Value [3]	0.0119

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

3. Primary: Change From Baseline in Maximum Walking Distance (MWD) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Primary
Measure Title	Change From Baseline in Maximum Walking Distance (MWD)
Measure Description	No text entered.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=those participants with observed data at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Change From Baseline in Maximum Walking Distance (MWD) [units: meters] Median (Inter-Quartile Range)	
Baseline; n=143	350.0 (200.0 to 1000)
Change from Baseline at Week 24; n=136	0.0 (0.0 to 170.0)
Change from Baseline at Week 48; n=129	0.0 (0.0 to 150.0)

Statistical Analysis 1 for Change From Baseline in Maximum Walking Distance (MWD)

Groups [1]	Natalizumab
Method [2]	Wilcoxon signed rank test
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Change From Baseline in Maximum Walking Distance (MWD)

Groups [1]	Natalizumab
Method [2]	Wilcoxon signed rank test
P Value [3]	0.0157

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

4. Primary: Change From Baseline in Expanded Disability Status Scale (EDSS) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Primary
Measure Title	Change From Baseline in Expanded Disability Status Scale (EDSS)
Measure Description	EDSS assesses disability in 8 functional systems. An overall score ranging from 0 (normal) to 10 (death due to MS) was calculated.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Change From Baseline in Expanded Disability Status Scale (EDSS) [units: units on a scale] Median (Inter-Quartile Range)	
Baseline; n=215	4.0 (2.5 to 5.0)
Change from Baseline at Week 24; n=207	0.0 (-0.5 to 0.0)
Change from Baseline at Week 48; n=199	0.0 (-0.5 to 0.0)

Statistical Analysis 1 for Change From Baseline in Expanded Disability Status Scale (EDSS)

Groups [1]	Natalizumab
Method [2]	Wilcoxon signed rank test
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Change From Baseline in Expanded Disability Status Scale (EDSS)

Groups [1]	Natalizumab
Method [2]	Wilcoxon signed rank test
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline, Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

5. Secondary: Correlation Between the EDSS and MWD (Pearson Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the EDSS and MWD (Pearson Correlation Coefficient)
Measure Description	Pearson correlation coefficient is a measure of the linear correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the EDSS and MWD (Pearson Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=143	-0.7245
Change from Baseline at Week 24; n=131	-0.6937
Change from Baseline at week 48; n=124	-0.4188

Statistical Analysis 1 for Correlation Between the EDSS and MWD (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the EDSS and MWD (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the EDSS and MWD (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

6. Secondary: Correlation Between the EDSS and MWD (Spearman Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the EDSS and MWD (Spearman Correlation Coefficient)
Measure Description	Spearman correlation coefficient is a non-parametric measure of the correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the EDSS and MWD (Spearman Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=143	-0.9197
Change from Baseline at Week 24; n=131	-0.6797
Change from Baseline at week 48; n=124	-0.5861

Statistical Analysis 1 for Correlation Between the EDSS and MWD (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the EDSS and MWD (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the EDSS and MWD (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

7. Secondary: Correlation Between the T100T and T25FW (Pearson Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the T100T and T25FW (Pearson Correlation Coefficient)
Measure Description	Pearson correlation coefficient is a measure of the linear correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the T100T and T25FW (Pearson Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=215	0.9235
Change from Baseline at Week 24; n=207	0.4752
Change from Baseline at week 48; n=199	0.4827

Statistical Analysis 1 for Correlation Between the T100T and T25FW (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the T100T and T25FW (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the T100T and T25FW (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

8. Secondary: Correlation Between the T100T and T25FW (Spearman Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the T100T and T25FW (Spearman Correlation Coefficient)
Measure Description	Spearman correlation coefficient is a non-parametric measure of the correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the T100T and T25FW (Spearman Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=215	0.8737
Change from Baseline at Week 24; n=207	0.5558
Change from Baseline at Week 48; n=199	0.4777

Statistical Analysis 1 for Correlation Between the T100T and T25FW (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the T100T and T25FW (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the T100T and T25FW (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

9. Secondary: Correlation Between the EDSS and T25FW (Pearson Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the EDSS and T25FW (Pearson Correlation Coefficient)
Measure Description	Pearson correlation coefficient is a measure of the linear correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the EDSS and T25FW (Pearson Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=215	0.5134
Change from Baseline at Week 24; n=207	0.1945
Change from Baseline at Week 48; n=199	0.1237

Statistical Analysis 1 for Correlation Between the EDSS and T25FW (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the EDSS and T25FW (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the EDSS and T25FW (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

10. Secondary: Correlation Between the EDSS and T25FW (Spearman Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the EDSS and T25FW (Spearman Correlation Coefficient)
Measure Description	Spearman correlation coefficient is a non-parametric measure of the correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the EDSS and T25FW (Spearman Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=215	0.7574
Change from Baseline at Week 24; n=207	0.2623
Change from Baseline at Week 48; n=199	0.2661

Statistical Analysis 1 for Correlation Between the EDSS and T25FW (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the EDSS and T25FW (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the EDSS and T25FW (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

11. Secondary: Correlation Between the EDSS and T100T (Pearson Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the EDSS and T100T (Pearson Correlation Coefficient)
Measure Description	Pearson correlation coefficient is a measure of the linear correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the EDSS and T100T (Pearson Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=215	0.5356
Change from Baseline at Week 24; n=207	0.2176
Change from Baseline at Week 48; n=199	0.1218

Statistical Analysis 1 for Correlation Between the EDSS and T100T (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the EDSS and T100T (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	0.0016

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the EDSS and T100T (Pearson Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Pearson Correlation
P Value [3]	0.0866

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

12. Secondary: Correlation Between the EDSS and T100T (Spearman Correlation Coefficient) [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Correlation Between the EDSS and T100T (Spearman Correlation Coefficient)
Measure Description	Spearman correlation coefficient is a non-parametric measure of the correlation (dependence) between 2 variables, giving a value between +1 and −1 inclusive, where 1 is total positive correlation, 0 is no correlation, and −1 is total negative correlation.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n=number of participants with data evaluated at given time point.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Measured Values

	Natalizumab
Number of Participants Analyzed [units: participants]	215
Correlation Between the EDSS and T100T (Spearman Correlation Coefficient) [units: Correlation coefficient]	
Baseline; n=215	0.7269
Change from Baseline at Week 24; n=207	0.3778
Change from Baseline at Week 48; n=199	0.2898

Statistical Analysis 1 for Correlation Between the EDSS and T100T (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Baseline
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Correlation Between the EDSS and T100T (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 24
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Correlation Between the EDSS and T100T (Spearman Correlation Coefficient)

Groups [1]	Natalizumab
Method [2]	Spearman correlation
P Value [3]	<0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from Baseline at Week 48
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

13. Secondary: Improvement in Timed 25FT Walk Speed and T100T Speed at Week 24 and 48 [Time Frame: Baseline, Week 24, Week 48]

Measure Type	Secondary
Measure Title	Improvement in Timed 25FT Walk Speed and T100T Speed at Week 24 and 48
Measure Description	To determine how well each of the walking tests, T100T or T25FW, predicts walking limitations, participants were stratified by baseline EDSS scores, and walking tests at Weeks 24 and 48 were analyzed. A 15% or 20% improvement indicates that, when compared with baseline walking speed (meters per second), there is at least 15% or 20% improvement at the corresponding timepoint, e.g. (speed at Week 24 – speed at baseline)/speed at baseline*100% ≥ 15% or 20%. Confirmed (conf) improvement at Week 48 indicates that the participant has at least 15% (or 20%) improvement in walking speed at both Week 24 and Week 48.
Time Frame	Baseline, Week 24, Week 48
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Efficacy Analysis Population (participants who had at least 1 infusion of natalizumab and completed at least 1 on-treatment evaluation); n= number of participants with evaluable data at time point.

Reporting Groups

	Description
Natalizumab: Baseline EDSS 0 to 2.5	natalizumab 300 mg IV every 4 weeks for 48 weeks in participants with a Baseline EDSS of 0 to 2.5
Natalizumab: Baseline EDSS 3.0 to 4.0	natalizumab 300 mg IV every 4 weeks for 48 weeks in participants with a Baseline EDSS 3.0 to 4.0
Natalizumab: Baseline EDSS >= 4.5	natalizumab 300 mg IV every 4 weeks for 48 weeks in participants with a Baseline EDSS >= 4.5

Measured Values

	Natalizumab: Baseline EDSS 0 to 2.5	Natalizumab: Baseline EDSS 3.0 to 4.0	Natalizumab: Baseline EDSS >= 4.5
Number of Participants Analyzed [units: participants]	53	74	80
Improvement in Timed 25FT Walk Speed and T100T Speed at Week 24 and 48 [units: participants]			
T25FW: 15% Improved at Week 24; n=53,74,80	6	11	19
T25FW: 15% Improved at Week 48; n=52,74,73	8	12	15
T25FW: 15% Improved at Week 48 conf; n=52,74,72	3	6	10
T25FW: 20% Improved at Week 24; n=52,74,80	5	8	14
T25FW: 20% Improved at Week 48; n=52,74,73	6	8	12
T25FW: 20% Improved at Week 48 conf; n=52,74,72	2	4	7
T100T: 15% Improved at Week 24; n=53,74,80	11	13	24
T100T: 15% Improved at Week 48; n=52,74,73	11	20	24
T100T: 15% Improved at Week 48 conf; n=52,74,72	7	12	21
T100T: 20% Improved at Week 24; n=53,74,80	10	10	18
T100T: 20% Improved at Week 48; n=52,74,73	9	17	23
T100T: 20% Improved at Week 48 conf; n=52,74,72	6	9	16

No statistical analysis provided for Improvement in Timed 25FT Walk Speed and T100T Speed at Week 24 and 48

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Day 1 (Baseline) through Week 48 (± 7 days) plus 4 weeks (± 7 days) follow-up
Additional Description	No text entered.

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Serious Adverse Events

	Natalizumab
Total, serious adverse events	
# participants affected / at risk	7/218 (3.21%)
Blood and lymphatic system disorders	
Leukopenia † 1	
# participants affected / at risk	1/218 (0.46%)
Cardiac disorders	
Aortic valve stenosis † 1	
# participants affected / at risk	1/218 (0.46%)
General disorders	
Sudden death † 1	
# participants affected / at risk	1/218 (0.46%)
Immune system disorders	
Anaphylactic reaction † 1	
# participants affected / at risk	1/218 (0.46%)
Infections and infestations	
Pneumonia † 1	
# participants affected / at risk	1/218 (0.46%)
Sepsis † 1	
# participants affected / at risk	1/218 (0.46%)
Nervous system disorders	
Multiple sclerosis relapse † 1	
# participants affected / at risk	1/218 (0.46%)
Renal and urinary disorders	
Calculus ureteric † 1	
# participants affected / at risk	1/218 (0.46%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 17.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Day 1 (Baseline) through Week 48 (± 7 days) plus 4 weeks (± 7 days) follow-up
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Natalizumab	natalizumab 300 mg IV every 4 weeks for 48 weeks

Other Adverse Events

	Natalizumab
Total, other (not including serious) adverse events	
# participants affected / at risk	28/218 (12.84%)
Infections and infestations	
Upper respiratory tract infection † 1	
# participants affected / at risk	18/218 (8.26%)
Nervous system disorders	
Headache † 1	
# participants affected / at risk	14/218 (6.42%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 17.0

Limitations and Caveats

Hide Limitations and Caveats

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

More Information

Hide More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.
There IS an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days. The sponsor cannot require changes to the communication and cannot extend the embargo. The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is more than 60 days but less than or equal to 180 days. The

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

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

☑ Restriction Description: 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:

Name/Title: Biogen Idec Study Medical Director
Organization: Biogen Idec
e-mail: clinicaltrials@biogenidec.com

No publications provided

Responsible Party:	Biogen Idec
ClinicalTrials.gov Identifier:	NCT00871780 History of Changes
Other Study ID Numbers:	TYS-IMA-08-11
Study First Received:	March 26, 2009
Results First Received:	November 11, 2014
Last Updated:	November 11, 2014
Health Authority:	Romania: National Authority for Scientific Research Belgium: Federal Agency for Medicinal Products and Health Products Romania: National Medicines Agency Belgium: The Federal Public Service (FPS) Health, Food Chain Safety and Environment Mexico: National Institute of Public Health, Health Secretariat Romania: Ministry of Public Health Mexico: Federal Commission for Protection Against Health Risks Mexico: National Council of Science and Technology Saudi Arabia: Research Advisory Council Mexico: Federal Commission for Sanitary Risks Protection Poland: Ministry of Health Belgium: Ministry of Social Affairs, Public Health and the Environment Saudi Arabia: Ministry of Health Mexico: Ethics Committee Belgium: Institutional Review Board Romania: State Institute for Drug Control Mexico: Ministry of Health Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Poland: Ministry of Science and Higher Education Belgium: Federal Agency for Medicines and Health Products, FAMHP Ukraine: Ministry of Health Ukraine: State Pharmacological Center - Ministry of Health