Safety and Efficacy Study of Daclizumab High Yield Process (DAC HYP) to Treat Relapsing-Remitting Multiple Sclerosis (SELECT)

This study has been completed.

Sponsor:
Biogen

Collaborator:
AbbVie

Information provided by (Responsible Party):
Biogen

ClinicalTrials.gov Identifier:
NCT00390221

First received: October 17, 2006
Last updated: May 31, 2016
Last verified: May 2016
History of Changes

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Results First Received: May 31, 2016

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Relapsing-Remitting Multiple Sclerosis
Interventions:	Biological: BIIB019 (Daclizumab High Yield Process) Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

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

Pre-Assignment Details

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

Reporting Groups

	Description
Placebo	Placebo administered as 3 subcutaneous (SC) injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg Daclizumab High Yield Process (DAC HYP) administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Participant Flow: Overall Study

	Placebo	**150 mg DAC HYP**	**300 mg DAC HYP**
STARTED	**204**	**208**	**209**

COMPLETED	**186**	**188**	**194**
NOT COMPLETED	**18**	**20**	**15**
Lost to Follow-up	**0**	**3**	**0**
Adverse Event	**1**	**4**	**3**
Investigator Decision	**0**	**0**	**1**
Withdrawal by Subject	**13**	**9**	**7**
Subject Non-compliance	**1**	**0**	**2**
Not Specified	**3**	**4**	**2**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

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

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
Total	Total of all reporting groups

Baseline Measures

	Placebo	**150 mg DAC HYP**	**300 mg DAC HYP**	**Total**
Number of Participants [units: participants]	**204**	**208**	**209**	**621**
Age [units: years] Mean (Standard Deviation)	**36.6 (9.02)**	**35.3 (8.94)**	**35.2 (8.67)**	**35.7 (8.88)**
Age, Customized [units: participants]				
18 to 19 years	**1**	**4**	**5**	**10**
20 to 29 years	**46**	**55**	**53**	**154**
30 to 39 years	**79**	**73**	**90**	**242**
40 to 49 years	**60**	**67**	**49**	**176**
50 to 55 years	**18**	**9**	**12**	**39**
Gender [units: participants]				
Female	**128**	**140**	**134**	**402**
Male	**76**	**68**	**75**	**219**

Outcome Measures

Hide All Outcome Measures

1. Primary: Adjusted Annualized Relapse Rate Between Baseline and Week 52 [Time Frame: Baseline through Week 52]

Measure Type	Primary
Measure Title	Adjusted Annualized Relapse Rate Between Baseline and Week 52
Measure Description	Relapses are defined as new or recurrent neurologic symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the examining neurologist. The annualized relapse rate was calculated as the total number of relapses that occurred during the study divided by the total number of subject-years followed in the study.
Time Frame	Baseline through Week 52
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.
Intent to treat population: all randomized participants who received at least 1 dose of study medication (excluding 21 participants from a single site due to a protocol violation in dosing).

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Measured Values

	Placebo	**150 mg DAC HYP**	**300 mg DAC HYP**
Number of Participants Analyzed [units: participants]	**196**	**201**	**203**
Adjusted Annualized Relapse Rate Between Baseline and Week 52 [units: relapses per person-years] Number (95% Confidence Interval)	**0.458 (0.370 to 0.566)**	**0.211 (0.155 to 0.287)**	**0.230 (0.172 to 0.308)**

Statistical Analysis 1 for Adjusted Annualized Relapse Rate Between Baseline and Week 52

Groups [1]	Placebo vs. 150 mg DAC HYP
Method [2]	Negative Binomial Regression
P Value [3]	<0.0001
Rate Ratio [4]	0.461
95% Confidence Interval	0.318 to 0.668

[1]	Additional details about the analysis, such as null hypothesis and power calculation:

	No text entered.
[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:
	adjusted for the number of relapses in the 1 year prior to study entry, baseline Expanded Disability Status Scale (<=2.5 vs > 2.5), and age (<=35 vs >35)
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Adjusted Annualized Relapse Rate Between Baseline and Week 52

Groups [1]	Placebo vs. 300 mg DAC HYP
Method [2]	Negative Binomial Regression
P Value [3]	0.0002
Rate Ratio [4]	0.503
95% Confidence Interval	0.352 to 0.721

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[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:
	adjusted for the number of relapses in the 1 year prior to study entry, baseline Expanded Disability Status Scale (<=2.5 vs > 2.5), and age (<=35 vs >35)
[4]	Other relevant estimation information:
	No text entered.

2. Secondary: Adjusted Mean Number of New Gadolinium (Gd)-Enhancing Lesions Between Week 8 and Week 24 [Time Frame: Week 8 through Week 24]

Measure Type	Secondary
Measure Title	Adjusted Mean Number of New Gadolinium (Gd)-Enhancing Lesions Between Week 8 and Week 24
Measure Description	Gd-enhancing lesions are detected when Gd leaks into a perivascular space due to local breakdown of the blood-brain barrier, indicating the presence of active inflammation. For participants with missing data the last valid nonbaseline measurement was carried forward if the participant was missing only 1 or 2 consecutive postbaseline scans. Otherwise the mean based on treatment group and visit was used as the imputed value. Estimated from a negative binomial model adjusted for the baseline number of Gd-enhancing lesions.
Time Frame	Week 8 through Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Magnetic Resonance Imaging (MRI) Intensive Population: a protocol-defined subset of participants consisting of the first 307 participants enrolled in the study with non-missing baseline values.

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Measured Values

	Placebo	**150 mg DAC HYP**	**300 mg DAC HYP**
Number of Participants Analyzed [units: participants]	**104**	**101**	**102**
Adjusted Mean Number of New Gadolinium (Gd)-Enhancing Lesions Between Week 8 and Week 24 [units: lesions] Mean (95% Confidence Interval)	**4.79 (3.56 to 6.43)**	**1.46 (1.05 to 2.03)**	**1.03 (0.73 to 1.46)**

Statistical Analysis 1 for Adjusted Mean Number of New Gadolinium (Gd)-Enhancing Lesions Between Week 8 and Week 24

Groups [1]	Placebo vs. 300 mg DAC HYP
Method [2]	Negative Binomial Regression
P Value [3]	<0.0001
Percent Reduction [4]	78.44
95% Confidence Interval	65.97 to 86.35

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	adjusted for the baseline number of Gd-enhancing lesions
[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]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Adjusted Mean Number of New Gadolinium (Gd)-Enhancing Lesions Between Week 8 and Week 24

Groups [1]	Placebo vs. 150 mg DAC HYP

Method [2]	Negative Binomial Regression
P Value [3]	<0.0001
Percent Reduction [4]	69.47
95% Confidence Interval	52.40 to 80.41

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	adjusted for the baseline number of Gd-enhancing lesions
[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]	Other relevant estimation information:
	No text entered.

3. Secondary: Adjusted Mean Number of New or Newly-enlarging T2 Hyperintense Lesions at Week 52 [Time Frame: Week 52]

Measure Type	Secondary
Measure Title	Adjusted Mean Number of New or Newly-enlarging T2 Hyperintense Lesions at Week 52
Measure Description	Lesions detected on T2-weighted sequences represent a range of histopathology related to MS, including edema, inflammation, demyelination, gliosis, and axon loss.
Time Frame	Week 52
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.
Intent to treat population: all randomized subjects who received at least 1 dose of study medication (excluding 21 subjects from a single site due to a protocol violation in dosing) with a non-missing value at baseline.

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Measured Values

	Placebo	150 mg DAC HYP	300 mg DAC HYP

Number of Participants Analyzed [units: participants]	**195**	**199**	**200**
Adjusted Mean Number of New or Newly-enlarging T2 Hyperintense Lesions at Week 52 [units: lesions] Mean (95% Confidence Interval)	**8.13 (6.65 to 9.94)**	**2.42 (1.96 to 2.99)**	**1.73 (1.39 to 2.15)**

Statistical Analysis 1 for Adjusted Mean Number of New or Newly-enlarging T2 Hyperintense Lesions at Week 52

Groups [1]	Placebo vs. 300 mg DAC HYP
Method [2]	Negative Binomial Regression
P Value [3]	<0.0001
Percent Reduction [4]	78.73
95% Confidence Interval	71.33 to 84.22

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	adjusted for baseline number of T2 lesions
[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]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Adjusted Mean Number of New or Newly-enlarging T2 Hyperintense Lesions at Week 52

Groups [1]	Placebo vs. 150 mg DAC HYP
Method [2]	Negative Binomial Regression
P Value [3]	<0.0001
Percent Reduction [4]	70.23
95% Confidence Interval	59.94 to 77.88

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	adjusted for baseline number of T2 lesions
[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]	Other relevant estimation information:
	No text entered.

4. Secondary: Proportion of Participants Who Relapsed at Week 52 [Time Frame: Week 52]

Measure Type	Secondary
Measure Title	Proportion of Participants Who Relapsed at Week 52
Measure Description	Estimated cumulative proportion of participants relapsed at Week 52, based on the Kaplan-Meier product limit method. Only relapses confirmed by the Independent Neurology Evaluation Committee were included in the analysis.
Time Frame	Week 52
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.
Intent to treat population: all randomized subjects who received at least 1 dose of study medication (excluding 21 subjects from a single site due to a protocol violation in dosing). Participants who did not experience a relapse prior to switching to alternative MS medications or withdrawal from study were censored.

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Measured Values

	Placebo	**150 mg DAC HYP**	**300 mg DAC HYP**
Number of Participants Analyzed [units: participants]	**196**	**201**	**203**
Proportion of Participants Who Relapsed at Week 52 [units: proportion of participants]	**0.36**	**0.19**	**0.20**

Statistical Analysis 1 for Proportion of Participants Who Relapsed at Week 52

Groups [1]	Placebo vs. 300 mg DAC HYP
Method [2]	Cox Proportional Hazard
P Value [3]	0.0003
Hazard Ratio [4]	0.49
95% Confidence Interval	0.33 to 0.72

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[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:
	Covariates included were number of relapses in the 1 year prior to study entry (p=0.001), baseline Expanded Disability Status Scale (<=2.5 versus >2.5, p=0.449), and age (<=35 versus >35, p=0.026).
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Proportion of Participants Who Relapsed at Week 52

Groups [1]	Placebo vs. 150 mg DAC HYP
Method [2]	Cox Proportional Hazard
P Value [3]	<0.0001
Hazard Ratio (HR) [4]	0.45
95% Confidence Interval	0.30 to 0.67

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[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:
	Covariates included were number of relapses in the 1 year prior to study entry (p=0.001), baseline Expanded Disability Status Scale (<=2.5 versus >2.5, p=0.449), and age (<=35 versus >35, p=0.026).
[4]	Other relevant estimation information:
	No text entered.

5. Secondary: Mean Change From Baseline in Multiple Sclerosis Impact Scale (MSIS)-29 Physical Impact Score at Week 52 [Time Frame: Baseline and Week 52]

Measure Type	Secondary
Measure Title	Mean Change From Baseline in Multiple Sclerosis Impact Scale (MSIS)-29 Physical Impact Score at Week 52
Measure Description	The 29-item Multiple Sclerosis Impact Scale (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. Responses use a 5 point Likert scale range from

	1 to 5. All questions are to be answered. The total score is the sum of points for all 29 questions, with a minimum score of 29, and a maximum score of 145. A lower total score indicates less physically-related impact while a higher total score indicates greater physically-related impact on a subject's functioning.
Time Frame	Baseline and Week 52
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.
Intent to treat population: all randomized subjects who received at least 1 dose of study medication (excluding 21 subjects from a single site due to a protocol violation in dosing).

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Measured Values

	Placebo	**150 mg DAC HYP**	**300 mg DAC HYP**
Number of Participants Analyzed [units: participants]	**196**	**201**	**203**
Mean Change From Baseline in Multiple Sclerosis Impact Scale (MSIS)-29 Physical Impact Score at Week 52 [units: units on a scale] Mean (Standard Deviation)	**3.0 (13.52)**	**-1.0 (11.80)**	**1.4 (13.53)**

Statistical Analysis 1 for Mean Change From Baseline in Multiple Sclerosis Impact Scale (MSIS)-29 Physical Impact Score at Week 52

Groups [1]	Placebo vs. 300 mg DAC HYP
Method [2]	Analysis of Variance
P Value [3]	0.1284
Relative Mean Change [4]	-1.93
95% Confidence Interval	-4.42 to 0.56

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[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:

	Analysis of variance for difference between treatment groups, controlling for baseline score.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Mean Change From Baseline in Multiple Sclerosis Impact Scale (MSIS)-29 Physical Impact Score at Week 52

Groups [1]	Placebo vs. 150 mg DAC HYP
Method [2]	Analysis of Variance
P Value [3]	0.0008
Relative Mean Change [4]	-4.27
95% Confidence Interval	-6.76 to -1.78

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	For each of the secondary endpoints, a sequential closed testing procedure was used, with the first comparison (the DAC HYP 300 mg group versus placebo) and the second comparison (the DAC HYP 150 mg group versus placebo). Secondary endpoints were rank prioritized, in the order presented. If statistical significance was not achieved for an endpoint, all endpoints(s) of a lower rank were not considered statistically significant.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Analysis of variance for difference between treatment groups, controlling for baseline score.
[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]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	AEs and SAEs were collected from the Screening Visit (≤ 21 Days prior to Baseline) through the Follow-Up Visit (Week 72 ± 5 days) or early discontinuation.
Additional Description	No text entered.

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
Total Active	150 mg or 300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Serious Adverse Events

	Placebo	150 mg DAC HYP	300 mg DAC HYP	Total Active

Total, serious adverse events				
# participants affected / at risk	**53/204 (25.98%)**	**32/208 (15.38%)**	**36/209 (17.22%)**	**68/417 (16.31%)**
Blood and lymphatic system disorders				
Leukocytosis † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Lymphadenopathy † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Cardiac disorders				
Angina unstable † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Atrial fibrillation † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Myocardial ischaemia † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Endocrine disorders				
Autoimmune thyroiditis † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Diabetes insipidus † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Eye disorders				
Retinal vein occlusion † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Gastrointestinal disorders				
Colitis ischaemic † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Crohn's disease † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Gastritis † 1				
# participants affected / at risk	**1/204 (0.49%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Gastroduodenitis † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Gastrooesophageal reflux disease † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Hepatobiliary disorders				
Cholecystitis chronic † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Cholelithiasis † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Hepatitis toxic † 1				

# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Jaundice † 1				
# participants affected / at risk	0/204 (0.00%)	0/208 (0.00%)	1/209 (0.48%)	1/417 (0.24%)
Immune system disorders				
Hypersensitivity † 1				
# participants affected / at risk	0/204 (0.00%)	0/208 (0.00%)	1/209 (0.48%)	1/417 (0.24%)
Infections and infestations				
Appendicitis † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Chronic Hepatitis B † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Cytomegalovirus infection † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Gastroenteritis † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Peritonsillar abscess † 1				
# participants affected / at risk	0/204 (0.00%)	0/208 (0.00%)	1/209 (0.48%)	1/417 (0.24%)
Psoas abscess † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Sinusitis † 1				
# participants affected / at risk	0/204 (0.00%)	0/208 (0.00%)	1/209 (0.48%)	1/417 (0.24%)
Urinary tract infection † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Viral infection † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Yersinia infection † 1				
# participants affected / at risk	0/204 (0.00%)	0/208 (0.00%)	1/209 (0.48%)	1/417 (0.24%)
Injury, poisoning and procedural complications				
Brain contusion † 1				
# participants affected / at risk	1/204 (0.49%)	0/208 (0.00%)	0/209 (0.00%)	0/417 (0.00%)
Contusion † 1				
# participants affected / at risk	1/204 (0.49%)	0/208 (0.00%)	0/209 (0.00%)	0/417 (0.00%)
Femoral neck fracture † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Tibia fracture † 1				
# participants affected / at risk	1/204 (0.49%)	0/208 (0.00%)	0/209 (0.00%)	0/417 (0.00%)
Investigations				
Alanine aminotransferase increased † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)
Aspartate aminotransferase increased † 1				
# participants affected / at risk	0/204 (0.00%)	1/208 (0.48%)	0/209 (0.00%)	1/417 (0.24%)

Metabolism and nutrition disorders				
Hypercholesterolaemia † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Hyperglycaemia † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Musculoskeletal and connective tissue disorders				
Back pain † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Cervix carcinoma † 1				
# participants affected / at risk	**1/204 (0.49%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Malignant melanoma † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Superficial spreading melanoma stage unspecified † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Nervous system disorders				
Cerebrovascular insufficiency † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Intracranial aneurysm † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Migraine † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Multiple sclerosis † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Multiple sclerosis relapse † 1				
# participants affected / at risk	**44/204 (21.57%)**	**19/208 (9.13%)**	**18/209 (8.61%)**	**37/417 (8.87%)**
Syncope † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Temporal lobe epilepsy † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Pregnancy, puerperium and perinatal conditions				
Abortion missed † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Psychiatric disorders				
Mood disorder due to a general medical condition † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Renal and urinary disorders				
Nephrolithiasis † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**

Reproductive system and breast disorders				
Cervical dysplasia † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Dysfunctional uterine bleeding † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Endometrial hyperplasia † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Ovarian cyst † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Ovarian disorder † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Uterine polyp † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Respiratory, thoracic and mediastinal disorders				
Pleurisy † 1				
# participants affected / at risk	**1/204 (0.49%)**	**0/208 (0.00%)**	**0/209 (0.00%)**	**0/417 (0.00%)**
Skin and subcutaneous tissue disorders				
Dermatitis allergic † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Dermatitis atopic † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Dermatitis exfoliative † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Erythema nodosum † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**
Rash † 1				
# participants affected / at risk	**0/204 (0.00%)**	**1/208 (0.48%)**	**0/209 (0.00%)**	**1/417 (0.24%)**
Vascular disorders				
Circulatory collapse † 1				
# participants affected / at risk	**0/204 (0.00%)**	**0/208 (0.00%)**	**1/209 (0.48%)**	**1/417 (0.24%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 16.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	AEs and SAEs were collected from the Screening Visit (≤ 21 Days prior to Baseline) through the Follow-Up Visit (Week 72 ± 5 days) or early discontinuation.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Placebo	Placebo administered as 3 SC injections every 4 weeks for up to 52 weeks
150 mg DAC HYP	150 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
300 mg DAC HYP	300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks
Total Active	150 mg or 300 mg DAC HYP administered as 3 SC injections every 4 weeks for up to 52 weeks

Other Adverse Events

	Placebo	150 mg DAC HYP	300 mg DAC HYP	Total Active
Total, other (not including serious) adverse events				
# participants affected / at risk	**128/204 (62.75%)**	**109/208 (52.40%)**	**111/209 (53.11%)**	**220/417 (52.76%)**
General disorders				
Pyrexia † 1				
# participants affected / at risk	**2/204 (0.98%)**	**7/208 (3.37%)**	**15/209 (7.18%)**	**22/417 (5.28%)**
Infections and infestations				
Influenza † 1				
# participants affected / at risk	**11/204 (5.39%)**	**5/208 (2.40%)**	**12/209 (5.74%)**	**17/417 (4.08%)**
Nasopharyngitis † 1				
# participants affected / at risk	**31/204 (15.20%)**	**30/208 (14.42%)**	**30/209 (14.35%)**	**60/417 (14.39%)**
Oral herpes † 1				
# participants affected / at risk	**10/204 (4.90%)**	**10/208 (4.81%)**	**13/209 (6.22%)**	**23/417 (5.52%)**
Pharyngitis † 1				
# participants affected / at risk	**9/204 (4.41%)**	**13/208 (6.25%)**	**13/209 (6.22%)**	**26/417 (6.24%)**
Respiratory tract infection † 1				
# participants affected / at risk	**11/204 (5.39%)**	**7/208 (3.37%)**	**13/209 (6.22%)**	**20/417 (4.80%)**
Upper respiratory tract infection † 1				
# participants affected / at risk	**14/204 (6.86%)**	**18/208 (8.65%)**	**22/209 (10.53%)**	**40/417 (9.59%)**
Investigations				
Alanine aminotransferase increased † 1				
# participants affected / at risk	**4/204 (1.96%)**	**9/208 (4.33%)**	**12/209 (5.74%)**	**21/417 (5.04%)**
Nervous system disorders				
Headache † 1				
# participants affected / at risk	**21/204 (10.29%)**	**20/208 (9.62%)**	**20/209 (9.57%)**	**40/417 (9.59%)**
Multiple sclerosis relapse † 1				
# participants affected / at risk	**73/204 (35.78%)**	**45/208 (21.63%)**	**38/209 (18.18%)**	**83/417 (19.90%)**
Psychiatric disorders				
Depression † 1				
# participants affected / at risk	**3/204 (1.47%)**	**10/208 (4.81%)**	**12/209 (5.74%)**	**22/417 (5.28%)**
Skin and subcutaneous tissue disorders				

Rash † 1				
# participants affected / at risk	**6/204 (2.94%)**	**11/208 (5.29%)**	**11/209 (5.26%)**	**22/417 (5.28%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 16.1

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 Study Medical Director
Organization: Biogen
e-mail: clinicaltrials@biogen.com

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Huss DJ, Mehta DS, Sharma A, You X, Riester KA, Sheridan JP, Amaravadi LS, Elkins JS, Fontenot JD. In vivo maintenance of human regulatory T cells during CD25 blockade. J Immunol. 2015 Jan 1;194(1):84-92.

Gold R, Giovannoni G, Selmaj K, Havrdova E, Montalban X, Radue EW, Stefoski D, Robinson R, Riester K, Rana J, Elkins J, O'Neill G; SELECT study investigators. Daclizumab high-yield process in relapsing-remitting multiple sclerosis (SELECT): a randomised, double-blind, placebo-controlled trial. Lancet. 2013 Jun 22;381(9884):2167-75. doi: 10.1016/S0140-6736(12)62190-4. Epub 2013 Apr 4.

Responsible Party: Biogen
ClinicalTrials.gov Identifier: NCT00390221 History of Changes

Other Study ID Numbers:	**205-MS-201**
Study First Received:	October 17, 2006
Results First Received:	May 31, 2016
Last Updated:	May 31, 2016
Health Authority:	Ukraine: State Pharmacological Center - Ministry of Health Czech Republic: State Institute for Drug Control Hungary: National Institute of Pharmacy United Kingdom: Medicines and Healthcare Products Regulatory Agency Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products India: Drugs Controller General of India Turkey: Ministry of Health Germany: Paul-Ehrlich-Institut Russia: Ministry of Health of the Russian Federation