Clinical trial results:
Antelope: Efficacy and Safety of the Biosimilar Natalizumab PB006 in Comparison to Tysabri® in Patients with Relapsing-Remitting Multiple Sclerosis (RRMS)

Summary

EudraCT number	2018-004751-20
Trial protocol	PL HR
Global end of trial date	23 August 2021

Results information

Result version number	v1 (current)
This version publication date	29 March 2022
First version publication date	29 March 2022

Trial information

Trial identification

Sponsor protocol code	PB006-03-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04115488
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Polpharma Biologics S.A.
Sponsor organisation address	ul. Trzy Lipy 3, Gdańsk, Poland, 80-172
Public contact	Karsten Roth, Director Clinical Research and Development, Polpharma Biologics S.A., +48 607 697 896, clinicaltrials@polpharmabiologics.com
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2021
Global end of trial reached?	Yes
Global end of trial date	23 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate and compare the cumulative number of new active lesions

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all subjects as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 59
Country: Number of subjects enrolled	Croatia: 2
Country: Number of subjects enrolled	Belarus: 49
Country: Number of subjects enrolled	Moldova, Republic of: 2
Country: Number of subjects enrolled	Serbia: 24
Country: Number of subjects enrolled	Ukraine: 99
Country: Number of subjects enrolled	Georgia: 30
Worldwide total number of subjects	265
EEA total number of subjects	61

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	265
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a Phase 3 multicenter, double-blind, active-controlled, randomized, parallel-group study to assess the similarity in efficacy, safety, and immunogenicity of biosimilar natalizumab PB006 compared to European Union-approved Tysabri in patients with Relapsing-remitting multiple sclerosis (RRMS).

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	PB006

Arm description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of PB006 at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions.

Arm type	Experimental
Investigational medicinal product name	PB006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of PB006 at a dose of 300 milligram (mg).

Arm title	Tysabri

Arm description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. Patients re-randomized and switched from Tysabri to PB006 at Week 24 still received a total of 12 infusions (6 infusions of Tysabri and 6 infusions of PB006).

Arm type	Active comparator
Investigational medicinal product name	Tysabri
Investigational medicinal product code	
Other name	natalizumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg).

Investigational medicinal product name	PB006
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of PB006 at a dose of 300 milligram (mg).

Number of subjects in period 1[1]	PB006	Tysabri
Started	131	133
Completed	117	122
Not completed	14	11
Adverse event, non-fatal	8	4
Other than listed	6	7

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of the 265 enrolled subjects, 264 were randomized.

Baseline characteristics

Reporting groups

Reporting group title	PB006

Reporting group description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of PB006 at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions.

Reporting group title	Tysabri

Reporting group description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. Patients re-randomized and switched from Tysabri to PB006 at Week 24 still received a total of 12 infusions (6 infusions of Tysabri and 6 infusions of PB006).

Reporting group values	PB006	Tysabri	Total
Number of subjects	131	133	264
Age categorical			
The Full Analysis Set (FAS) Population includes all patients who were randomized and have received at least one infusion of the study drug.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	131	133	264
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
The Full Analysis Set (FAS) Population includes all patients who were randomized and have received at least one infusion of the study drug.			
Units: years			
arithmetic mean	36.8	9.73	
standard deviation	± 9.05	± 37.0	-
Gender categorical			
The Full Analysis Set (FAS) Population includes all patients who were randomized and have received at least one infusion of the study drug.			
Units: Subjects			
Female	84	78	162
Male	47	55	102
Race (NIH/OMB)			
The Full Analysis Set (FAS) Population includes all patients who were randomized and have received at least one infusion of the study drug.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Black or African American	0	0	0

Asian	0	0	0
White	131	133	264
Native Hawaiian or Other Pacific Islander	0	0	0
Not reported	0	0	0
Other	0	0	0
Ethnicity (NIH/OMB)			
The Full Analysis Set (FAS) Population includes all patients who were randomized and have received at least one infusion of the study drug.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	131	133	264
Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	PB006

Reporting group description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of PB006 at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions.

Reporting group title	Tysabri

Reporting group description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. Patients re-randomized and switched from Tysabri to PB006 at Week 24 still received a total of 12 infusions (6 infusions of Tysabri and 6 infusions of PB006).

Subject analysis set title	PB006 (SSW)
Subject analysis set type	Per protocol

Subject analysis set description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of PB006 at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions.
Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switched or not.

Subject analysis set title	Tysabri Switched to PB006 at week 24 (SSW)
Subject analysis set type	Per protocol

Subject analysis set description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. Patients re-randomized and switched from Tysabri to PB006 at Week 24 still received a total of 12 infusions (6 infusions of Tysabri and 6 infusions of PB006). This arm concerns patients who started on Tysabri and continued on PB006 following the re-randomization at week 24.
Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switched or not.

Subject analysis set title	Tysabri continued at week 24 (SSW)
Subject analysis set type	Per protocol

Subject analysis set description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. This arm concerns patients who started on Tysabri and continued on Tysabri following the re-randomization at week 24. Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switched or not.

Subject analysis set title	PB006 (SAF)
Subject analysis set type	Per protocol

Subject analysis set description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of PB006 at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Subject analysis set title	Tysabri Switched to PB006 at week 24 (SAF)
Subject analysis set type	Per protocol

Subject analysis set description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. Patients re-randomized and switched from Tysabri to PB006 at Week 24 still received a total of 12 infusions (6 infusions of Tysabri and 6 infusions of PB006). This arm concerns patients who started on Tysabri and continued on PB006 following the re-randomization at week 24. Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Subject analysis set title	Tysabri continued at week 24 (SAF)
Subject analysis set type	Per protocol

Subject analysis set description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received IV infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. This arm concerns patients who started on Tysabri and continued on Tysabri following the re-randomization at week 24. Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Primary: Cumulative number of new active lesions over 24 weeks

End point title	Cumulative number of new active lesions over 24 weeks

End point description:

Cumulative number of new active lesions over 24 weeks, calculated as the sum of all new gadolinium-enhancing (GdE) T1-weighted and new/enlarging T2-weighted lesion. Assessment was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted and T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center.

Per-Protocol Population (PP): patients who completed the 24-week treatment period without major protocol deviations that may have influenced the analysis of the primary endpoint and for whom sufficient post-baseline MRI data were available (incl baseline, Week 24 and at least 1/3 MRI visits).

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switched or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Primary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20 and 24.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	126[1]	127[2]	122[3]	30[4]
Units: lesions				
arithmetic mean (standard deviation)	1.4 (± 3.73)	1.9 (± 3.97)	1.4 (± 3.65)	2.1 (± 3.78)

Notes:

[1] - PP

[2] - PP

[3] - SSW

[4] - SSW

End point values	Tysabri			

	continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[5]			
Units: lesions				
arithmetic mean (standard deviation)	1.9 (± 4.09)			

Notes:

[5] - SSW

Statistical analyses

Statistical analysis title	Primary Efficacy Analysis

Statistical analysis description:

Data was analyzed using a negative binomial model with a logarithmic link function and fixed effects for the treatment group and stratification factors. Equivalence was tested based 95% confidence interval. Difference calculated as Tysabri minus PB006.

Comparison groups	PB006 v Tysabri
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Exponentiated Difference
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.613
upper limit	0.944
Variability estimate	Standard error of the mean
Dispersion value	0.397

Secondary: Cumulative number of new active lesions over 48 weeks

End point title	Cumulative number of new active lesions over 48 weeks

End point description:

Cumulative number of new active lesions over 48 weeks, calculated as the sum of all new gadolinium-enhancing (GdE) T1-weighted and new/enlarging T2-weighted lesion. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted lesions and T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center. A macrocyclic Gd-based contrast agent was administered as an Intravenous infusion of 0.1 Millimole per kilogram [mmol/kg].

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.
Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20, 24 and 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	122[6]	96[7]	119[8]	29[9]
Units: Lesions				
arithmetic mean (standard deviation)	1.5 (± 3.72)	2.3 (± 5.68)	1.5 (± 3.75)	2.1 (± 3.82)

Notes:

[6] - FAS

[7] - FAS, patients who switch from Tysabri to PB006 are excluded.

[8] - SSW

[9] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[10]			
Units: Lesions				
arithmetic mean (standard deviation)	2.3 (± 5.70)			

Notes:

[10] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of new GdE T1-weighted lesions over 24 weeks

End point title	Cumulative number of new GdE T1-weighted lesions over 24 weeks

End point description:

Cumulative number of new GdE T1-weighted lesions over 24 weeks, calculated as the sum of all new gadolinium-enhancing (GdE) T1-weighted. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center. A macrocyclic Gd-based contrast agent (gadobutrol, gadoteric acid, or gadoteridol) was to be administered as an Intravenous infusion of 0.1 Millimole per kilogram [mmol/kg].

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.
Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20 and 24.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	126[11]	127[12]	122[13]	30[14]
Units: Lesions				
arithmetic mean (standard deviation)	0.3 (± 1.01)	0.4 (± 1.25)	0.3 (± 1.02)	0.4 (± 0.81)

Notes:

[11] - FAS

[12] - FAS

[13] - FAS

[14] - FAS

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[15]			
Units: Lesions				
arithmetic mean (standard deviation)	0.4 (± 1.37)			

Notes:

[15] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of new GdE T1-weighted lesions over 48 weeks

End point title	Cumulative number of new GdE T1-weighted lesions over 48 weeks

End point description:

Cumulative number of new GdE T1-weighted lesions over 48 weeks, calculated as the sum of all new gadolinium-enhancing (GdE) T1-weighted. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center. A macrocyclic Gd-based contrast agent (gadobutrol, gadoteric acid, or gadoteridol) was to be administered as an Intravenous infusion of 0.1 Millimole per kilogram [mmol/kg].

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20, 24 and 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	122[16]	96[17]	119[18]	29[19]
Units: Lesions				
arithmetic mean (standard deviation)	0.3 (± 1.02)	0.4 (± 1.39)	0.3 (± 1.03)	0.4 (± 0.82)

Notes:

[16] - FAS

[17] - FAS

[18] - SSW

[19] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[20]			
Units: Lesions				
arithmetic mean (standard deviation)	0.4 (± 1.40)			

Notes:

[20] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients without new GdE T1-weighted lesions over 24 weeks

End point title	Number of patients without new GdE T1-weighted lesions over 24 weeks

End point description:

Number of patients without new GdE T1-weighted lesions over 24 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center. A macrocyclic Gd-based contrast agent (gadobutrol, gadoteric acid, or gadoteridol) was to be administered as an Intravenous infusion of 0.1 Millimole per kilogram [mmol/kg].

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20 and 24.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	131[21]	133[22]	122[23]	30[24]
Units: Subjects	109	105	105	23

Notes:

[21] - FAS

[22] - FAS

[23] - SSW

[24] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[25]			
Units: Subjects	80			

Notes:

[25] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients without new GdE T1-weighted lesions over 48 weeks

End point title	Number of patients without new GdE T1-weighted lesions over 48 weeks

End point description:

Number of patients without new GdE T1-weighted lesions over 48 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center. A macrocyclic Gd-based contrast agent (gadobutrol, gadoteric acid, or gadoteridol) was to be administered as an Intravenous infusion of 0.1 Millimole per kilogram [mmol/kg].

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20, 24 and 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	131[26]	103[27]	122[28]	30[29]
Units: Subjects	105	80	102	22

Notes:

[26] - FAS

[27] - FAS, patients who switch from Tysabri to PB006 are excluded.

[28] - SSW

[29] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[30]			
Units: Subjects	79			

Notes:

[30] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of new/enlarging T2-weighted lesions over 24 weeks

End point title	Cumulative number of new/enlarging T2-weighted lesions over 24 weeks

End point description:

Cumulative number of new/enlarging T2-weighted lesions over 24 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20 and 24.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	126[31]	127[32]	122[33]	30[34]
Units: Lesions				
arithmetic mean (standard deviation)	1.5 (± 3.79)	2.0 (± 4.12)	1.5 (± 3.83)	2.2 (± 3.84)

Notes:

[31] - FAS

[32] - FAS

[33] - SSW

[34] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[35]			
Units: Lesions				
arithmetic mean (standard deviation)	2.0 (± 4.25)			

Notes:

[35] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative number of new/enlarging T2-weighted lesions over 48 weeks

End point title	Cumulative number of new/enlarging T2-weighted lesions over 48 weeks

End point description:

Cumulative number of new/enlarging T2-weighted lesions over 48 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20, 24 and 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	122[36]	96[37]	119[38]	29[39]
Units: Lesions				
arithmetic mean (standard deviation)	1.6 (± 3.90)	2.4 (± 5.79)	1.6 (± 3.93)	2.2 (± 3.89)

Notes:

[36] - FAS

[37] - FAS, patients who switch from Tysabri to PB006 are excluded.

[38] - SSW

[39] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[40]			
Units: Lesions				
arithmetic mean (standard deviation)	2.5 (± 5.81)			

Notes:

[40] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of persistent lesions after 24 weeks

End point title	Number of persistent lesions after 24 weeks

End point description:

Number of persistent lesions after 24 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted lesions and T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center. A macrocyclic Gd-based contrast agent (gadobutrol, gadoteric acid, or gadoteridol) was to be administered as an Intravenous infusion of 0.1 Millimole per kilogram [mmol/kg].

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20 and 24.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	126[41]	127[42]	122[43]	30[44]
Units: Lesions				
arithmetic mean (standard deviation)	0.5 (± 2.46)	0.4 (± 2.92)	0.5 (± 2.49)	0.1 (± 0.31)

Notes:

[41] - FAS

[42] - FAS

[43] - SSW

[44] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[45]			
Units: Lesions				

arithmetic mean (standard deviation)	0.6 (± 3.37)			

Notes:

[45] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of persistent lesions after 48 weeks

End point title	Number of persistent lesions after 48 weeks

End point description:

Number of persistent lesions after 48 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of GdE T1-weighted lesions and T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center. A macrocyclic Gd-based contrast agent (gadobutrol, gadoteric acid, or gadoteridol) was to be administered as an Intravenous infusion of 0.1 Millimole per kilogram [mmol/kg].

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20, 24 and 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	122[46]	96[47]	119[48]	29[49]
Units: Lesions				
arithmetic mean (standard deviation)	0.5 (± 2.55)	0.6 (± 3.35)	0.5 (± 2.58)	0.1 (± 0.26)

Notes:

[46] - FAS

[47] - FAS, patients who switch from Tysabri to PB006 are excluded.

[48] - SSW

[49] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[50]			
Units: Lesions				
arithmetic mean (standard deviation)	0.6 (± 3.37)			

Notes:
[50] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized relapse rate after 24 weeks

End point title	Annualized relapse rate after 24 weeks

End point description:

Annualized relapse rate after 24 weeks. Relapse was defined as the appearance of a new neurological abnormality or worsening of previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding clinical demyelinating event. The abnormality had to be present for at least 24 hours and have occurred in the absence of fever or infection.
Annualized relapse rate:
A: Number of medically confirmed relapses per patient. B: Duration of follow-up time per patient, defined as: (last day of follow-up - day of randomization + 1) / 365.25. Relapses per patient-year: A/B.

FAS: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.
SSW: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

End point type	Secondary

End point timeframe:

Up to 24 weeks.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	131[51]	133[52]	122[53]	30[54]
Units: Relapses per patient-year				
number (not applicable)	0.206	0.152	0.194	0.143

Notes:
[51] - FAS
[52] - FAS
[53] - SSW
[54] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[55]			
Units: Relapses per patient-year				
number (not applicable)	0.114			

Notes:
[55] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized relapse rate after 48 weeks

End point title	Annualized relapse rate after 48 weeks

End point description:

Annualized relapse rate after 48 weeks. Relapse was defined as the appearance of a new neurological abnormality or worsening of previously stable or improving pre-existing neurological abnormality, separated by at least 30 days from onset of a preceding clinical demyelinating event. The abnormality had to be present for at least 24 hours and have occurred in the absence of fever or infection.
Annualized relapse rate:
A: Number of medically confirmed relapses per patient. B: Duration of follow-up time per patient, defined as: (last day of follow-up - day of randomization + 1) / 365.25. Relapses per patient-year: A/B.

FAS: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.
SSW: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.
Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 48 weeks.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	131[56]	103[57]	122[58]	30[59]
Units: Relapses per patient-year				
number (not applicable)	0.174	0.133	0.168	0.146

Notes:
[56] - FAS
[57] - FAS, patients who switch from Tysabri to PB006 are excluded.
[58] - SSW
[59] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[60]			
Units: Relapses per patient-year				
number (not applicable)	0.113			

Notes:
[60] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Expanded Disability Status Scale (EDSS) after 24 weeks

End point title	Change from baseline in Expanded Disability Status Scale (EDSS) after 24 weeks

End point description:

Change from baseline in Expanded Disability Status Scale (EDSS) after 24 weeks. The Kurtzke EDSS, commonly used to evaluate the degree of neurologic impairment in multiple sclerosis (MS), is an ordinal clinical rating scale ranging from 0 (normal neurologic examination) to 10 (death due to MS) in half-point increments. Based on a standard neurological examination, the 7 functional systems (plus "other") are rated. These ratings are then used in conjunction with observations and information concerning gait and use of assistive devices to rate the EDSS. EDSS ratings were performed by independent examining neurologists. After re-randomization, Week 24 is considered baseline.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Baseline and week 24.

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122[61]	125[62]		
Units: Score on scale				
arithmetic mean (standard deviation)	-0.03 (± 0.211)	0.00 (± 0.354)		

Notes:
[61] - FAS
[62] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Expanded Disability Status Scale (EDSS) after 48 weeks

End point title	Change from baseline in Expanded Disability Status Scale (EDSS) after 48 weeks

End point description:

Change from baseline in Expanded Disability Status Scale (EDSS) after 48 weeks. The Kurtzke EDSS, commonly used to evaluate the degree of neurologic impairment in MS, is an ordinal clinical rating scale ranging from 0 (normal neurologic examination) to 10 (death due to MS) in half-point increments. Based

on a standard neurological examination, the 7 functional systems (plus "other") are rated. These ratings are then used in conjunction with observations and information concerning gait and use of assistive devices to rate the EDSS. EDSS ratings were performed by independent examining neurologists.

FAS population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

SSW Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

FAS: Baseline (week 0) and week 48.
SSW: Baseline (week 24) and week 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	117[63]	93[64]	117[65]	29[66]
Units: Score on scale				
arithmetic mean (standard deviation)	-0.14 (± 0.536)	-0.05 (± 0.443)	-0.10 (± 0.498)	-0.03 (± 0.325)

Notes:

[63] - FAS

[64] - FAS, patients who switch from Tysabri to PB006 are excluded.

[65] - SSW

[66] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	93[67]			
Units: Score on scale				
arithmetic mean (standard deviation)	-0.02 (± 0.312)			

Notes:

[67] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with anti-drug (natalizumab) antibodies (ADA) and persistent antibodies after 24 weeks

End point title	Percentage of subjects with anti-drug (natalizumab) antibodies (ADA) and persistent antibodies after 24 weeks

End point description:

Percentage of subjects with anti-drug (natalizumab) antibodies (ADA) and persistent antibodies after 24 weeks. A positive ADA patient was defined as a patient who had at least 1 positive ADA result in any

post-baseline sample. A persistently positive ADA patient was defined as a patient with confirmed positive ADAs in 2 or more consecutive positive ADA samples at post-dose visits.

Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 24 weeks.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	122[68]	125[69]	122[70]	30[71]
Units: Percentage of subjects				
number (not applicable)				
Persistently positive (confirmed)	28.7	27.2	28.7	43.3
Positive, confirmed	30.3	29.6	30.3	43.3

Notes:

[68] - SAF

[69] - SAF

[70] - SSW

[71] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[72]			
Units: Percentage of subjects				
number (not applicable)				
Persistently positive (confirmed)	22.1			
Positive, confirmed	25.3			

Notes:

[72] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with anti-drug (natalizumab) antibodies (ADA) and persistent antibodies after 48 weeks

End point title	Percentage of subjects with anti-drug (natalizumab) antibodies (ADA) and persistent antibodies after 48 weeks

End point description:

Percentage of subjects with anti-drug (natalizumab) antibodies (ADA) and persistent antibodies after 48 weeks. A positive ADA patient was defined as a patient who had at least 1 positive ADA result in any

post-baseline sample. A persistently positive ADA patient was defined as a patient with confirmed positive ADAs in 2 or more consecutive positive ADA samples at post-dose visits.

Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 48 weeks.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	115[73]	121[74]	115[75]	28[76]
Units: Percentage of subjects				
number (not applicable)				
Persistently positive (confirmed)	10.4	11.6	10.4	17.9
Positive, confirmed	11.3	11.6	11.3	17.9

Notes:

[73] - SAF

[74] - SAF

[75] - SSW

[76] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	93[77]			
Units: Percentage of subjects				
number (not applicable)				
Persistently positive (confirmed)	9.7			
Positive, confirmed	9.7			

Notes:

[77] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with neutralizing antibodies after 24 weeks

End point title	Percentage of subjects with neutralizing antibodies after 24 weeks

End point description:

Percentage of subjects with positive (transient and persistent) neutralizing antibodies after 24 weeks.

Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were

included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 24 weeks.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	37[78]	37[79]	37[80]	13[81]
Units: Percentage of subjects				
number (not applicable)				
Positive, confirmed	67.6	64.9	67.6	61.5

Notes:

[78] - SAF

[79] - SAF

[80] - SSW

[81] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	24[82]			
Units: Percentage of subjects				
number (not applicable)				
Positive, confirmed	66.7			

Notes:

[82] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with neutralizing antibodies after 48 weeks

End point title	Percentage of subjects with neutralizing antibodies after 48 weeks

End point description:

Percentage of subjects with positive (transient and persistent) neutralizing antibodies after 48 weeks.

Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 48 weeks.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	13[83]	14[84]	13[85]	5[86]
Units: Percentage of subjects				
number (not applicable)				
Positive, confirmed	61.5	50.0	61.5	60.0

Notes:

[83] - SAF

[84] - SAF

[85] - SSW

[86] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	9[87]			
Units: Percentage of subjects				
number (not applicable)				
Positive, confirmed	44.4			

Notes:

[87] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any Treatment-Emergent Adverse Event (TEAE) or any Treatment-Emergent Serious Adverse Event (SAE) after 24 weeks

End point title	Number of subjects with any Treatment-Emergent Adverse Event (TEAE) or any Treatment-Emergent Serious Adverse Event (SAE) after 24 weeks

End point description:

Number of subjects with any Treatment-Emergent Adverse Event (TEAE) or any Treatment-Emergent Serious Adverse Event (SAE) after 24 weeks.
Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

End point type	Secondary

End point timeframe:

Up to week 24

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131[88]	133[89]		
Units: Subjects				
TEAE	62	64		
Treatment-emergent SAE	1	0		

Notes:

[88] - SAF

[89] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any Treatment-Emergent Adverse Event (TEAE) or any Treatment-Emergent Serious Adverse Event (SAE) after 48 weeks

End point title	Number of subjects with any Treatment-Emergent Adverse Event (TEAE) or any Treatment-Emergent Serious Adverse Event (SAE) after 48 weeks

End point description:

Number of subjects with any Treatment-Emergent Adverse Event (TEAE) or any Treatment-Emergent Serious Adverse Event (SAE) after 48 weeks. Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

End point type	Secondary

End point timeframe:

Up to 48 weeks.

End point values	PB006 (SAF)	Tysabri Switched to PB006 at week 24 (SAF)	Tysabri continued at week 24 (SAF)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	131[90]	30[91]	103[92]	
Units: Subjects				
TEAE	85	22	71	
Treatment-emergent SAE	3	0	2	

Notes:

[90] - SAF

[91] - SAF

[92] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Natalizumab trough concentration (Ctrough) over time, week 8

End point title	Natalizumab trough concentration (Ctrough) over time, week 8

End point description:

Natalizumab trough concentration (Ctrough) over time, week 8. Serum samples were collected prior to treatment.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Week 8

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118[93]	125[94]		
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	26804.75 (± 12949.541)	25010.49 (± 12557.895)		

Notes:

[93] - FAS

[94] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Natalizumab trough concentration (Ctrough) over time, week 16

End point title	Natalizumab trough concentration (Ctrough) over time, week 16

End point description:

Natalizumab trough concentration (Ctrough) over time, week 16. Serum samples were collected prior to treatment.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Week 16

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117[95]	122[96]		
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	33872.92 (± 18151.190)	32543.28 (± 14636.925)		

Notes:

[95] - FAS

[96] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Natalizumab trough concentration (Ctrough) over time, week 24

End point title	Natalizumab trough concentration (Ctrough) over time, week 24

End point description:

Natalizumab trough concentration (Ctrough) over time, week 24. Serum samples were collected prior to treatment.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117[97]	121[98]		
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	36853.93 (± 15292.389)	35617.65 (± 16049.669)		

Notes:

[97] - FAS

[98] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Natalizumab trough concentration (Ctrough) over time, week 32

End point title	Natalizumab trough concentration (Ctrough) over time, week 32

End point description:

Natalizumab trough concentration (Ctrough) over time, week 32. Serum samples were collected prior to treatment.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Week 32

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115[99]	94[100]		
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	37450.04 (± 16877.010)	36865.81 (± 19756.050)		

Notes:

[99] - FAS

[100] - FAS, patients who switch from Tysabri to PB006 are excluded.

Statistical analyses

No statistical analyses for this end point

Secondary: Natalizumab trough concentration (Ctrough) over time, week 48

End point title	Natalizumab trough concentration (Ctrough) over time, week 48

End point description:

Natalizumab trough concentration (Ctrough) over time, week 48. Serum samples were collected prior to treatment.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Week 48

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110[101]	91[102]		
Units: Nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	39097.58 (± 16801.710)	38432.86 (± 16495.407)		

Notes:

[101] - FAS

[102] - FAS, patients who switch from Tysabri to PB006 are excluded.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients without new/enlarging T2-weighted lesions over 24 weeks

End point title	Number of patients without new/enlarging T2-weighted lesions over 24 weeks

End point description:

Number of patients without new/enlarging T2-weighted lesions over 24 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

End point type	Secondary

End point timeframe:

Week 0 (baseline), week 8, 16, 20 and 24.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	131[103]	133[104]	122[105]	30[106]
Units: Subjects	75	72	72	18

Notes:

[103] - FAS

[104] - FAS

[105] - SSW

[106] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[107]			
Units: Subjects	52			

Notes:

[107] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients without new/enlarging T2-weighted lesions over 48 weeks

End point title	Number of patients without new/enlarging T2-weighted lesions over 48 weeks

End point description:

Number of patients without new/enlarging T2-weighted lesions over 48 weeks. Assessment of lesions was performed using Magnetic Resonance Imaging (MRI). Identification of T2-weighted lesions was done by a trained and certified radiology reviewer according to standard procedures at the MRI central reading center.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switch or not.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

Scans performed at week 0 (baseline), week 8, 16, 20, 24 and 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	131[108]	103[109]	122[110]	30[111]
Units: Subjects	71	52	69	17

Notes:

[108] - FAS

[109] - FAS, patients who switch from Tysabri to PB006 are excluded.

[110] - SSW

[111] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[112]			
Units: Subjects	51			

Notes:

[112] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal clinical laboratory tests at week 24 and week 48

End point title	Number of patients with abnormal clinical laboratory tests at week 24 and week 48

End point description:

Number of patients with abnormal clinical laboratory tests at week 24 and 48.

The Full Analysis Set (FAS) population: patients who were randomized and have received at least one (complete or partial) infusion of the study drug.

Safety-Switch (SSW) Population: treated patients who received at least one infusion of the study drug after the time point of re-randomization, independent of whether they switched or not.

End point type	Secondary

End point timeframe:

At week 24 and week 48.

End point values	PB006	Tysabri	PB006 (SSW)	Tysabri Switched to PB006 at week 24 (SSW)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	131[113]	133[114]	122[115]	30[116]
Units: Subjects				
Week 24	116	114	116	27
Week 48	108	88	108	26

Notes:

[113] - FAS

[114] - FAS, patients who switch from Tysabri to PB006 are excluded at week 48.

[115] - SSW

[116] - SSW

End point values	Tysabri continued at week 24 (SSW)			
Subject group type	Subject analysis set			
Number of subjects analysed	95[117]			
Units: Subjects				
Week 24	87			
Week 48	88			

Notes:

[117] - SSW

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal findings in physical examination at week 24 and week 48

End point title	Number of patients with abnormal findings in physical examination at week 24 and week 48

End point description:

Number of patients with abnormal findings in physical examination at week 24 and week 48.
Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF).

End point type	Secondary

End point timeframe:

Week 24 and end of study (week 48).

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131[118]	133[119]		
Units: Subjects				
Week 24	10	12		
End of study (week 48)	11	10		

Notes:
[118] - SAF
[119] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in blood pressure at week 24

End point title	Change from baseline in blood pressure at week 24

End point description:

Change from baseline in diastolic and systolic blood Pressure at week 24.
Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF).

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

At baseline and week 24.

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122[120]	125[121]		
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)				
Diastolic Blood Pressure	-2.2 (± 7.30)	-0.6 (± 7.35)		
Systolic Blood Pressure	-1.0 (± 9.76)	-1.5 (± 11.33)		

Notes:
[120] - SAF
[121] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in blood pressure at week 48

End point title	Change from baseline in blood pressure at week 48

End point description:

Change from baseline in diastolic and systolic blood Pressure at week 48.
Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF).

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

At baseline and end of study (week 48).

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117[122]	93[123]		
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)	-1.1 (± 8.84)	0.4 (± 8.54)		

Notes:

[122] - SAF

[123] - SAF, patients who switch from Tysabri to PB006 are excluded.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in heart rate at week 24

End point title	Change from baseline in heart rate at week 24

End point description:

Change from baseline in heart rate at week 24.
Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF). Patients in this group were analyzed as treated.

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

At baseline and week 24.

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122[124]	125[125]		
Units: beats/minute				
arithmetic mean (standard deviation)	-0.4 (± 9.05)	-1.4 (± 9.10)		

Notes:

[124] - SAF

[125] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in heart rate at week 48

End point title	Change from baseline in heart rate at week 48

End point description:

Change from baseline in heart rate at week 48.

Safety Population: Patients who received at least 1 (complete or partial) infusion of the study drug were included in the Safety Population (SAF).

Only subjects with non-missing endpoints were included in the analysis.

End point type	Secondary

End point timeframe:

At baseline and end of study (week 48).

End point values	PB006	Tysabri		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117[126]	93[127]		
Units: beats/minute				
arithmetic mean (standard deviation)	0.2 (± 9.74)	-0.3 (± 9.52)		

Notes:

[126] - SAF

[127] - SAF, patients who switch from Tysabri to PB006 are excluded.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first infusion till the last + 4 weeks, up to 48 weeks.
Deaths (all causes): From first infusion till the last (at Week 44) + 24 ± 2 weeks, up to 68 ± 2 weeks.

Adverse event reporting additional description:

Patients participating in this study who receive at least one (complete or partial) infusion of the study drug were included in the Safety Population (SAF).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	PB006

Reporting group description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of PB006 at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. Included in this arm are subjects who switched from Tysabri to PB006 at week 24, covering the period from week 24 till the end of study (week 48).

Reporting group title	Tysabri

Reporting group description:

Patients with relapsing-remitting multiple sclerosis (RRMS) received intravenous (IV) infusions every 4 weeks of Tysabri at a dose of 300 milligram (mg) starting at Visit 1 (Week 0) through Visit 12 (Week 44), for a total of 12 infusions. At Week 24, patients in the Tysabri group were re-randomized through a re-randomization step. Patients re-randomized and switched from Tysabri to PB006 at Week 24 still received a total of 12 infusions (6 infusions of Tysabri and 6 infusions of PB006). Included in this arm are subjects who switched from Tysabri to PB006 at week 24, covering the period from week 0 till week 24.

Serious adverse events	PB006	Tysabri	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 161 (1.86%)	2 / 133 (1.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Tremor			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Nasal septum deviation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	PB006	Tysabri	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 161 (62.11%)	93 / 133 (69.92%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Haemangioma of spleen			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Blood pressure fluctuation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	

Hypotension			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Thrombophlebitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 161 (3.11%)	2 / 133 (1.50%)	
occurrences (all)	5	2	
Fatigue			
subjects affected / exposed	5 / 161 (3.11%)	1 / 133 (0.75%)	
occurrences (all)	5	1	
Pyrexia			
subjects affected / exposed	1 / 161 (0.62%)	4 / 133 (3.01%)	
occurrences (all)	1	4	
Hyperthermia			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Feeling hot			
subjects affected / exposed	1 / 161 (0.62%)	2 / 133 (1.50%)	
occurrences (all)	1	2	
Oedema peripheral			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Discomfort			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Infusion site pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			

Dysmenorrhoea			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Menorrhagia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Metrorrhagia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Organic erectile dysfunction			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	5 / 161 (3.11%)	3 / 133 (2.26%)	
occurrences (all)	5	3	
Rhinitis allergic			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Rhinorrhoea			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Allergic sinusitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Catarrh			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Paranasal sinus mucosal hypertrophy			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Depression			
subjects affected / exposed	4 / 161 (2.48%)	4 / 133 (3.01%)	
occurrences (all)	4	4	
Insomnia			
subjects affected / exposed	4 / 161 (2.48%)	1 / 133 (0.75%)	
occurrences (all)	6	1	
Sleep disorder			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Somatic symptom disorder			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Investigations			
Weight decreased			
subjects affected / exposed	2 / 161 (1.24%)	4 / 133 (3.01%)	
occurrences (all)	2	4	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	2	
Blood pressure increased			
subjects affected / exposed	1 / 161 (0.62%)	2 / 133 (1.50%)	
occurrences (all)	1	2	
C-reactive protein increased			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	2	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Bilirubin conjugated increased			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Blood triglycerides increased			

subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	2	0	
Lymphocyte count increased			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 161 (0.00%)	2 / 133 (1.50%)	
occurrences (all)	0	2	
Ankle fracture			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Limb injury			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Muscle injury			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Scar			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Nervous system disorders			

Headache			
subjects affected / exposed	27 / 161 (16.77%)	23 / 133 (17.29%)	
occurrences (all)	38	52	
Dizziness			
subjects affected / exposed	3 / 161 (1.86%)	3 / 133 (2.26%)	
occurrences (all)	3	4	
Hypoaesthesia			
subjects affected / exposed	3 / 161 (1.86%)	2 / 133 (1.50%)	
occurrences (all)	3	2	
Paraesthesia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Presyncope			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Tension headache			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	4	3	
Burning sensation			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Head titubation			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Hyposmia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Multiple sclerosis relapse			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	2	
Muscle spasticity			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	

Trigeminal neuralgia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 161 (2.48%)	0 / 133 (0.00%)	
occurrences (all)	4	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Lymphadenitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Normocytic anaemia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Ocular discomfort			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Visual impairment			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	3 / 161 (1.86%)	5 / 133 (3.76%)	
occurrences (all)	3	5	
Nausea			
subjects affected / exposed	4 / 161 (2.48%)	3 / 133 (2.26%)	
occurrences (all)	4	3	
Constipation			
subjects affected / exposed	2 / 161 (1.24%)	3 / 133 (2.26%)	
occurrences (all)	2	4	
Vomiting			
subjects affected / exposed	0 / 161 (0.00%)	2 / 133 (1.50%)	
occurrences (all)	0	2	
Abdominal pain			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	2	0	
Chronic gastritis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	2	
Dyspepsia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Large intestine polyp			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Pancreatitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	

Stomatitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Hyperbilirubinaemia			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Alopecia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Erythema			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Hyperhidrosis			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	2 / 161 (1.24%)	0 / 133 (0.00%)	
occurrences (all)	2	0	
Angioedema			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Idiopathic angioedema			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Petechiae			

subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Skin depigmentation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	0 / 161 (0.00%)	2 / 133 (1.50%)	
occurrences (all)	0	2	
Dysuria			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Nephroptosis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Renal pain			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Urinary tract inflammation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	7 / 161 (4.35%)	4 / 133 (3.01%)	
occurrences (all)	7	4	
Pain in extremity			
subjects affected / exposed	2 / 161 (1.24%)	3 / 133 (2.26%)	
occurrences (all)	2	3	
Muscle spasms			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Myalgia			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Neck pain			
subjects affected / exposed	1 / 161 (0.62%)	2 / 133 (1.50%)	
occurrences (all)	2	2	
Arthralgia			
subjects affected / exposed	2 / 161 (1.24%)	0 / 133 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 161 (0.00%)	2 / 133 (1.50%)	
occurrences (all)	0	2	
Arthritis reactive			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc disorder			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	2	0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	14 / 161 (8.70%)	13 / 133 (9.77%)	
occurrences (all)	19	14	
COVID-19			

subjects affected / exposed	14 / 161 (8.70%)	10 / 133 (7.52%)	
occurrences (all)	14	10	
Upper respiratory tract infection			
subjects affected / exposed	2 / 161 (1.24%)	4 / 133 (3.01%)	
occurrences (all)	2	4	
Pharyngitis			
subjects affected / exposed	1 / 161 (0.62%)	4 / 133 (3.01%)	
occurrences (all)	2	5	
Respiratory tract infection			
subjects affected / exposed	2 / 161 (1.24%)	2 / 133 (1.50%)	
occurrences (all)	2	2	
Urinary tract infection			
subjects affected / exposed	2 / 161 (1.24%)	2 / 133 (1.50%)	
occurrences (all)	2	3	
Bronchitis			
subjects affected / exposed	1 / 161 (0.62%)	3 / 133 (2.26%)	
occurrences (all)	1	4	
Cystitis			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Oral herpes			
subjects affected / exposed	2 / 161 (1.24%)	2 / 133 (1.50%)	
occurrences (all)	2	2	
Pneumonia			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Rhinitis			
subjects affected / exposed	1 / 161 (0.62%)	2 / 133 (1.50%)	
occurrences (all)	1	2	
Herpes simplex			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Respiratory tract infection viral			
subjects affected / exposed	2 / 161 (1.24%)	1 / 133 (0.75%)	
occurrences (all)	2	1	
Sinusitis			

subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Vaginal infection			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Acute sinusitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
COVID-19 pneumonia			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Ear infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Fungal skin infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Furuncle			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Helicobacter gastritis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Infected fistula			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	2	
Laryngitis			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Pyelonephritis acute			

subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Pyoderma streptococcal			
subjects affected / exposed	1 / 161 (0.62%)	1 / 133 (0.75%)	
occurrences (all)	1	1	
Tinea versicolour			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	2	
Hyperlipidaemia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 161 (0.00%)	1 / 133 (0.75%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	1 / 161 (0.62%)	0 / 133 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2019	The section about Overall Study Design has been revised to show that serum samples for anti-drug antibody (ADA) formation testing will now be collected at 2 additional time points: 4 Weeks and 28 Weeks.
05 February 2020	The sections Secondary Objectives, Overall Study Design, Secondary Endpoints, Statistical Methods, Secondary endpoints and Planned Sample Size have been updated to include the new study design of switching a group of patients from Tysabri to PB006 at Week 24 to evaluate and compare the immunogenic profiles of those on Tysabri only with those who switched.
15 July 2020	In order to simplify Clinical Study Reporting, the analysis of the primary endpoint will now be conducted together with all secondary endpoints at the end of the study (at Visit 13, Week 48). The primary endpoint itself (at Visit 7, Week 24) is not changed. Most protocol changes in this amendment relate to this simplification

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported