Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Vedolizumab in the Prophylaxis of Intestinal Acute Graft-Versus-Host Disease in Subjects Undergoing Allogeneic Hematopoietic Stem Cell Transplantation

Summary

EudraCT number	2018-002141-11
Trial protocol	HU SE GB NO DE AT PL ES PT BE GR IT RO Outside EU/EEA
Global end of trial date	09 May 2022

Results information

Result version number	v2
This version publication date	12 January 2023
First version publication date	02 December 2022
Version creation reason	• Correction of full data set Correction on MedDRA version used

Trial information

Trial identification

Sponsor protocol code	Vedolizumab-3035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03657160
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	40 Landsdowne Street, Cambridge, United States, MA 02139
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000645-PIP03-18
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the efficacy of vedolizumab when added to background aGvHD prophylaxis regimen compared to placebo and background aGvHD prophylaxis regimen on intestinal aGvHD-free survival by Day +180 in participants who receive allo-HSCT as treatment for a hematologic malignancy or myeloproliferative disorder.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy:

Intestinal acute graft-versus-host disease (aGvHD) prophylaxis regimen.

Evidence for comparator: -

Actual start date of recruitment	06 February 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	United States: 109
Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Japan: 37

Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Norway: 10
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	343
EEA total number of subjects	112

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)	1
Adults (18-64 years)	264
From 65 to 84 years	78
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 95 investigative sites in Canada, United States, Argentina, Brazil, Belgium, France, Germany, Italy, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom, Austria, Greece, Hungary, Poland, Israel, Romania, Russia, Australia, Japan, Republic of Korea and Singapore from 6 February 2019 to 9 May 2022.

Pre-assignment

Screening details:

Participants undergoing allogeneic hematopoietic stem cell transplantation (Allo-HSCT) were randomized into 1:1 ratio to receive Vedolizumab 300 mg or vedolizumab-matching placebo.

Pre-assignment period milestones

Number of subjects started	343
Number of subjects completed	333

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol Deviation: 1
Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Consent withdrawn by subject: 3
Reason: Number of subjects	Reason not Specified: 5

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Vedolizumab placebo-matching, intravenous (IV) infusion, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab placebo-matching intravenous infusion.

Arm title	Vedolizumab 300 mg

Arm description:

Vedolizumab 300 mg, IV, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.

Arm type	Experimental

Investigational medicinal product name	Vedolizumab
Investigational medicinal product code	
Other name	MLN0002
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vedolizumab intravenous infusion.

Number of subjects in period 1[1]	Placebo	Vedolizumab 300 mg
Started	165	168
Completed	98	116
Not completed	67	52
Unsatisfactory Therapeutic Response	5	3
Adverse event, serious fatal	33	26
Consent withdrawn by subject	17	14
Adverse event, non-fatal	4	6
Protocol Deviation	3	-
Site Terminated	1	-
Death (COVID-19-Related)	1	-
Other Reasons COVID-19-Related	-	1
Reason not Specified	3	2

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: 10 participants from 343 participants were randomized but did not continue the study.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Vedolizumab placebo-matching, intravenous (IV) infusion, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.	
Reporting group title	Vedolizumab 300 mg
Reporting group description:	
Vedolizumab 300 mg, IV, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.	

Reporting group values	Placebo	Vedolizumab 300 mg	Total
Number of subjects	165	168	
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.9	50.8	
standard deviation	± 14.49	± 14.41	-
Gender categorical Units: Subjects			
Male			0
Female			0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	9	16	25
Not Hispanic or Latino	133	133	266
Unknown or Not Reported	23	19	42
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	36	29	65
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	3	5
White	114	121	235
More than one race	0	0	0
Unknown or Not Reported	13	15	28
Gender Units: Subjects			
Male	106	103	209
Female	59	65	124

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Vedolizumab placebo-matching, intravenous (IV) infusion, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.	
Reporting group title	Vedolizumab 300 mg
Reporting group description:	
Vedolizumab 300 mg, IV, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.	

Primary: Intestinal aGvHD-Free Survival After Allo-HSCT

End point title	Intestinal aGvHD-Free Survival After Allo-HSCT
End point description:	
Intestinal aGvHD Free Survival is the time from the date of first study drug administration (Day-1) to intestinal aGvHD event/death, where an event is defined as death due to any cause or Stage 1-4 intestinal involvement per Acute Graft versus-Host Disease Clinical Stage criteria. Data was censored for participants who have not had the intestinal aGvHD event or died or have had the event after pre-specified timing, e.g., last contact or Day +180 after allo HSCT whichever occurs first. FAS included all participants who were randomized, received at least 1 dose of the treatment, and under-went allo HSCT. 99 indicates that median was not estimable due to fewer number of participants with events.	
End point type	Primary
End point timeframe:	
From the date of first dose of study drug to first documented intestinal aGvHD or death, whichever occurs first up to Day +180	

End point values	Placebo	Vedolizumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: days				
median (full range (min-max))	99 (14 to 182)	99 (2 to 182)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vedolizumab 300 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.73

Secondary: Intestinal aGvHD-Free and Relapse-Free Survival

End point title	Intestinal aGvHD-Free and Relapse-Free Survival

End point description:

GvHD and Relapse Free Survival is the time from the date of first study drug administration (Day-1) to GvHD event/death/relapse, where an event is defined as death or aGvHD Grade 3-4 by modified Glucksberg criteria or chronic GvHD requiring system immunosuppression or relapse. Data was censored for participants who have not had the event or have had the event after pre-specified timing, e.g., last contact or Day +180 after allo HSCT whichever occurs first. FAS included all participants who were randomized, received at least 1 dose of the treatment, and under-went allo HSCT. 99 indicates that median was not estimable due to fewer number of participants with events.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug to first documented intestinal aGvHD or death, whichever occurs first up to Day +180

End point values	Placebo	Vedolizumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: days				
median (full range (min-max))	99 (13 to 182)	99 (17 to 182)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vedolizumab 300 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0243
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.96

Secondary: Grade C-D aGvHD-Free Survival

End point title	Grade C-D aGvHD-Free Survival

End point description:

GvHD and Relapse Free Survival is the time from the date of first study drug administration (Day-1) to GvHD event/death/relapse, where an event is defined as death or aGvHD Grade 3-4 by modified Glucksberg criteria or chronic GvHD requiring system immunosuppression or relapse. Data was censored for participants who have not had the event or have had the event after pre-specified timing, e.g., last contact or Day +180 after allo HSCT whichever occurs first. FAS included all participants who were randomized, received at least 1 dose of the treatment, and under-went allo HSCT. 99 indicates that median was not estimable due to fewer number of participants with events.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug to first documented intestinal aGvHD or death, whichever occurs first up to Day +180

End point values	Placebo	Vedolizumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: days				
median (full range (min-max))	99 (12 to 182)	99 (12 to 182)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vedolizumab 300 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0204
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.91

Secondary: Nonrelapse Mortality (NRM)

End point title	Nonrelapse Mortality (NRM)

End point description:

Non-relapse mortality is the time from the date of first study drug administration (Day-1) to death without occurrence of a relapse. Data was censored for participants who have not had the event or have had the event after pre-specified timing, e.g., last contact or Day +180 after allo HSCT whichever occurs first. FAS included all participants who were randomized, received at least 1 dose of the treatment, and under-went allo HSCT. 99 indicates that median was not estimable due to fewer number of participants with events.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug to first documented intestinal aGvHD or death, whichever occurs first up to Day +180

End point values	Placebo	Vedolizumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: days				
median (full range (min-max))	99 (14 to 182)	99 (19 to 182)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vedolizumab 300 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0668
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	1.04

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall Survival by Days +180 is the time from the date of first study drug administration (Day-1) to death from any cause. Data was censored for participants who have not had the event or have had the event after pre-specified timing, e.g., last contact or Day +180 after allo-HSCT whichever occurs first. FAS included all participants who were randomized, received at least 1 dose of the treatment, and under-went allo HSCT. 99 indicates that median was not estimable due to fewer number of participants with events.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug to first documented intestinal aGvHD or death, whichever occurs first up to Day +180

End point values	Placebo	Vedolizumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: days				
median (full range (min-max))	99 (14 to 182)	99 (19 to 182)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vedolizumab 300 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1458
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.17

Secondary: Grade B-D aGvHD-Free Survival

End point title	Grade B-D aGvHD-Free Survival

End point description:

Grade B-D aGvHD Survival is the time from the date of first study drug administration (Day-1) to aGvHD event or death, where an event is defined as death or grade B-D any organ involvement per IBMTR Severity Index for aGvHD. Data was censored for participants who have not had the event or have had the event after pre-specified timing, e.g., last contact or Day +180 after allo HSCT whichever occurs first. FAS included all participants who were randomized, received at least 1 dose of the treatment, and under-went allo HSCT. 99 indicates that median was not estimable due to fewer number of participants with events.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug to first documented intestinal aGvHD or death, whichever occurs first up to Day +180

End point values	Placebo	Vedolizumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	168		
Units: days				
median (full range (min-max))	99 (12 to 182)	99 (12 to 182)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vedolizumab 300 mg v Placebo
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0105
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.91

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug until the end of study (up to approximately 281 days)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment. Safety Population included all participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Vedolizumab placebo-matching, intravenous (IV) infusion, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.

Reporting group title	Vedolizumab 300 mg

Reporting group description:

Vedolizumab 300 mg, IV, once on Day -1 along with background graft-versus-host disease (GvHD) prophylaxis regimen prior to Allo-HSCT and once on Days +13, +41, +69, +97, +125, and +153 post Allo-HSCT.

Serious adverse events	Placebo	Vedolizumab 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	114 / 165 (69.09%)	120 / 169 (71.01%)	
number of deaths (all causes)	27	21	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma recurrent			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Minimal residual disease			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma recurrent			

subjects affected / exposed	2 / 165 (1.21%)	0 / 169 (0.00%)		
occurrences causally related to treatment / all	0 / 3	0 / 0		
deaths causally related to treatment / all	0 / 2	0 / 0		
Acute lymphocytic leukaemia recurrent				
subjects affected / exposed	1 / 165 (0.61%)	3 / 169 (1.78%)		
occurrences causally related to treatment / all	0 / 2	0 / 4		
deaths causally related to treatment / all	0 / 1	0 / 0		
Central nervous system leukaemia				
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Philadelphia positive acute lymphocytic leukaemia				
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Chronic myeloid leukaemia recurrent				
subjects affected / exposed	1 / 165 (0.61%)	3 / 169 (1.78%)		
occurrences causally related to treatment / all	0 / 1	1 / 4		
deaths causally related to treatment / all	0 / 0	0 / 1		
Acute myeloid leukaemia recurrent				
subjects affected / exposed	9 / 165 (5.45%)	9 / 169 (5.33%)		
occurrences causally related to treatment / all	0 / 13	0 / 10		
deaths causally related to treatment / all	0 / 4	0 / 1		
Chloroma				
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Lymphoma				
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Post transplant lymphoproliferative disorder				

subjects affected / exposed	2 / 165 (1.21%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	3 / 165 (1.82%)	5 / 169 (2.96%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
Myelofibrosis			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoma benign			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral T-cell lymphoma unspecified recurrent			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Shock haemorrhagic			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venoocclusive disease			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 165 (0.61%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	13 / 165 (7.88%)	13 / 169 (7.69%)	
occurrences causally related to treatment / all	0 / 15	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	3 / 165 (1.82%)	5 / 169 (2.96%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 3	0 / 5	
Disease progression			

subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyserositis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perforated ulcer			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Acute graft versus host disease in intestine			
subjects affected / exposed	16 / 165 (9.70%)	6 / 169 (3.55%)	
occurrences causally related to treatment / all	1 / 20	1 / 6	
deaths causally related to treatment / all	0 / 2	0 / 0	
Acute graft versus host disease in liver			
subjects affected / exposed	2 / 165 (1.21%)	5 / 169 (2.96%)	
occurrences causally related to treatment / all	1 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute graft versus host disease			

subjects affected / exposed	5 / 165 (3.03%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute graft versus host disease in skin			
subjects affected / exposed	4 / 165 (2.42%)	3 / 169 (1.78%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease			
subjects affected / exposed	1 / 165 (0.61%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in liver			
subjects affected / exposed	2 / 165 (1.21%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Engraftment syndrome			
subjects affected / exposed	2 / 165 (1.21%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in eye			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute graft versus host disease oral			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in			

lung			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in skin			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease oral			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in lung			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
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			
Respiratory distress			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis obliterans syndrome			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			

subjects affected / exposed	3 / 165 (1.82%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epiglottic oedema			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pneumonia syndrome			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal oedema			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 165 (0.61%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	3 / 165 (1.82%)	5 / 169 (2.96%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 3	
Acute Respiratory failure			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 165 (0.00%)	3 / 169 (1.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Pseudomonas test positive			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blast cell count increased			

subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	4 / 165 (2.42%)	9 / 169 (5.33%)	
occurrences causally related to treatment / all	1 / 4	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 165 (0.61%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase abnormal			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Subdural haematoma			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prescribed overdose			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Engraft failure			
subjects affected / exposed	0 / 165 (0.00%)	4 / 169 (2.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant failure			
subjects affected / exposed	1 / 165 (0.61%)	3 / 169 (1.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delayed engraftment			

subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failures			
subjects affected / exposed	2 / 165 (1.21%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiopulmonary failure			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			

subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ventricular tachycardia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hemorrhage intracranial			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ataxia			
subjects affected / exposed	2 / 165 (1.21%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous sinus thrombosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered state of consciousness			

subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 165 (1.21%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			

subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 165 (1.82%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenias			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 165 (0.61%)	5 / 169 (2.96%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplastic anaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	8 / 165 (4.85%)	7 / 169 (4.14%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thrombocytopenia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Vertigo positional			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Neutropenic colitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 165 (2.42%)	6 / 169 (3.55%)	
occurrences causally related to treatment / all	1 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	4 / 165 (2.42%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal food impaction			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 165 (0.61%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 165 (0.61%)	4 / 169 (2.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	4 / 165 (2.42%)	5 / 169 (2.96%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choleostasis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	4 / 165 (2.42%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Autoimmune hepatitis			

subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	2 / 165 (1.21%)	4 / 169 (2.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute kidney injury			
subjects affected / exposed	8 / 165 (4.85%)	3 / 169 (1.78%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 165 (1.21%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in jaw			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Muscular weakness			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Enterocolitis infectious			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical mycobacterial infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acinetobacter infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal cellulitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			

subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural abscess			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection reactivation			
subjects affected / exposed	2 / 165 (1.21%)	6 / 169 (3.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			

subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection reactivation			
subjects affected / exposed	2 / 165 (1.21%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Escherichia infection			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis fungal			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 165 (0.61%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human herpesvirus 6 encephalitis			

subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 165 (1.21%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wound infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	8 / 165 (4.85%)	5 / 169 (2.96%)	
occurrences causally related to treatment / all	1 / 8	1 / 7	
deaths causally related to treatment / all	0 / 2	0 / 2	
Klebsiella sepsis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			

subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BK virus infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human polyomavirus infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonal			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			

subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	9 / 165 (5.45%)	4 / 169 (2.37%)	
occurrences causally related to treatment / all	1 / 13	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 0	
Bacteraemia			
subjects affected / exposed	5 / 165 (3.03%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	4 / 165 (2.42%)	4 / 169 (2.37%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic embolus			

subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic encephalopathy			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral toxoplasmosis			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	1 / 165 (0.61%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			

subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	1 / 165 (0.61%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 165 (0.00%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	2 / 165 (1.21%)	0 / 169 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 7	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 165 (0.00%)	1 / 169 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 165 (0.61%)	2 / 169 (1.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Vedolizumab 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	164 / 165 (99.39%)	169 / 169 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	54 / 165 (32.73%)	54 / 169 (31.95%)	
occurrences (all)	65	63	
Hypotension			
subjects affected / exposed	12 / 165 (7.27%)	19 / 169 (11.24%)	
occurrences (all)	13	21	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	62 / 165 (37.58%)	80 / 169 (47.34%)	
occurrences (all)	95	129	
Fatigue			
subjects affected / exposed	50 / 165 (30.30%)	38 / 169 (22.49%)	
occurrences (all)	64	51	
Oedema Peripheral			
subjects affected / exposed	35 / 165 (21.21%)	29 / 169 (17.16%)	
occurrences (all)	49	34	
Asthenia			
subjects affected / exposed	12 / 165 (7.27%)	14 / 169 (8.28%)	
occurrences (all)	16	14	
Chills			
subjects affected / exposed	10 / 165 (6.06%)	11 / 169 (6.51%)	
occurrences (all)	11	16	
Oedema			
subjects affected / exposed	13 / 165 (7.88%)	7 / 169 (4.14%)	
occurrences (all)	15	7	
Pain			
subjects affected / exposed	11 / 165 (6.67%)	4 / 169 (2.37%)	
occurrences (all)	11	4	
Immune system disorders			

Acute Graft Versus Host Disease in Skin			
subjects affected / exposed	65 / 165 (39.39%)	67 / 169 (39.64%)	
occurrences (all)	81	84	
Acute Graft Versus Host Disease In Intestine			
subjects affected / exposed	15 / 165 (9.09%)	10 / 169 (5.92%)	
occurrences (all)	15	15	
Chronic Graft Versus Host Disease Oral			
subjects affected / exposed	10 / 165 (6.06%)	14 / 169 (8.28%)	
occurrences (all)	11	17	
Chronic Graft Versus Host Disease In Skin			
subjects affected / exposed	7 / 165 (4.24%)	16 / 169 (9.47%)	
occurrences (all)	7	16	
Chronic Graft Versus Host Disease			
subjects affected / exposed	12 / 165 (7.27%)	10 / 169 (5.92%)	
occurrences (all)	12	10	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	25 / 165 (15.15%)	26 / 169 (15.38%)	
occurrences (all)	30	27	
Oropharyngeal Pain			
subjects affected / exposed	16 / 165 (9.70%)	25 / 169 (14.79%)	
occurrences (all)	16	27	
Dyspnoea			
subjects affected / exposed	22 / 165 (13.33%)	16 / 169 (9.47%)	
occurrences (all)	28	18	
Epistaxis			
subjects affected / exposed	17 / 165 (10.30%)	18 / 169 (10.65%)	
occurrences (all)	18	25	
Dyspnoea Exertional			
subjects affected / exposed	15 / 165 (9.09%)	7 / 169 (4.14%)	
occurrences (all)	16	10	
Rhinorrhoea			
subjects affected / exposed	9 / 165 (5.45%)	12 / 169 (7.10%)	
occurrences (all)	10	14	

Pneumonia			
subjects affected / exposed	9 / 165 (5.45%)	9 / 169 (5.33%)	
occurrences (all)	9	9	
Hypoxia			
subjects affected / exposed	11 / 165 (6.67%)	7 / 169 (4.14%)	
occurrences (all)	13	9	
Productive Cough			
subjects affected / exposed	9 / 165 (5.45%)	6 / 169 (3.55%)	
occurrences (all)	9	6	
Nasopharyngitis			
subjects affected / exposed	4 / 165 (2.42%)	9 / 169 (5.33%)	
occurrences (all)	6	11	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	32 / 165 (19.39%)	35 / 169 (20.71%)	
occurrences (all)	35	36	
Anxiety			
subjects affected / exposed	14 / 165 (8.48%)	14 / 169 (8.28%)	
occurrences (all)	14	15	
Depression			
subjects affected / exposed	6 / 165 (3.64%)	13 / 169 (7.69%)	
occurrences (all)	6	15	
Confusional State			
subjects affected / exposed	10 / 165 (6.06%)	3 / 169 (1.78%)	
occurrences (all)	10	3	
Investigations			
Platelet Count Decreased			
subjects affected / exposed	47 / 165 (28.48%)	38 / 169 (22.49%)	
occurrences (all)	56	52	
Alanine Aminotransferase Increased			
subjects affected / exposed	26 / 165 (15.76%)	36 / 169 (21.30%)	
occurrences (all)	34	53	
Blood Creatinine Increased			
subjects affected / exposed	35 / 165 (21.21%)	24 / 169 (14.20%)	
occurrences (all)	40	34	
Aspartate Aminotransferase Increased			

subjects affected / exposed	25 / 165 (15.15%)	30 / 169 (17.75%)	
occurrences (all)	27	40	
Blood Bilirubin Increased			
subjects affected / exposed	27 / 165 (16.36%)	21 / 169 (12.43%)	
occurrences (all)	27	25	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	15 / 165 (9.09%)	16 / 169 (9.47%)	
occurrences (all)	19	17	
Neutrophil Count Decreased			
subjects affected / exposed	15 / 165 (9.09%)	13 / 169 (7.69%)	
occurrences (all)	19	18	
White Blood Cell Count Decreased			
subjects affected / exposed	18 / 165 (10.91%)	10 / 169 (5.92%)	
occurrences (all)	21	13	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	9 / 165 (5.45%)	8 / 169 (4.73%)	
occurrences (all)	11	9	
Infusion Related Reaction			
subjects affected / exposed	3 / 165 (1.82%)	9 / 169 (5.33%)	
occurrences (all)	3	10	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	6 / 165 (3.64%)	12 / 169 (7.10%)	
occurrences (all)	9	13	
Nervous system disorders			
Headache			
subjects affected / exposed	58 / 165 (35.15%)	58 / 169 (34.32%)	
occurrences (all)	80	76	
Dizziness			
subjects affected / exposed	23 / 165 (13.94%)	21 / 169 (12.43%)	
occurrences (all)	33	23	
Dysgeusia			
subjects affected / exposed	21 / 165 (12.73%)	23 / 169 (13.61%)	
occurrences (all)	22	25	
Tremor			

subjects affected / exposed	21 / 165 (12.73%)	19 / 169 (11.24%)	
occurrences (all)	23	21	
Neuropathy Peripheral			
subjects affected / exposed	9 / 165 (5.45%)	10 / 169 (5.92%)	
occurrences (all)	10	11	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	72 / 165 (43.64%)	68 / 169 (40.24%)	
occurrences (all)	91	86	
Febrile Neutropenia			
subjects affected / exposed	54 / 165 (32.73%)	67 / 169 (39.64%)	
occurrences (all)	58	71	
Thrombocytopenia			
subjects affected / exposed	31 / 165 (18.79%)	43 / 169 (25.44%)	
occurrences (all)	42	54	
Neutropenia			
subjects affected / exposed	32 / 165 (19.39%)	40 / 169 (23.67%)	
occurrences (all)	38	46	
Eye disorders			
Dry Eye			
subjects affected / exposed	21 / 165 (12.73%)	34 / 169 (20.12%)	
occurrences (all)	25	36	
Vision Blurred			
subjects affected / exposed	11 / 165 (6.67%)	10 / 169 (5.92%)	
occurrences (all)	12	10	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	102 / 165 (61.82%)	95 / 169 (56.21%)	
occurrences (all)	141	142	
Stomatitis			
subjects affected / exposed	90 / 165 (54.55%)	90 / 169 (53.25%)	
occurrences (all)	102	104	
Nausea			
subjects affected / exposed	83 / 165 (50.30%)	85 / 169 (50.30%)	
occurrences (all)	110	109	
Vomiting			

subjects affected / exposed	55 / 165 (33.33%)	41 / 169 (24.26%)	
occurrences (all)	75	58	
Constipation			
subjects affected / exposed	47 / 165 (28.48%)	43 / 169 (25.44%)	
occurrences (all)	53	48	
Abdominal Pain			
subjects affected / exposed	35 / 165 (21.21%)	34 / 169 (20.12%)	
occurrences (all)	47	45	
Dry Mouth			
subjects affected / exposed	28 / 165 (16.97%)	27 / 169 (15.98%)	
occurrences (all)	31	32	
Dyspepsia			
subjects affected / exposed	20 / 165 (12.12%)	13 / 169 (7.69%)	
occurrences (all)	22	13	
Abdominal Pain Upper			
subjects affected / exposed	16 / 165 (9.70%)	16 / 169 (9.47%)	
occurrences (all)	19	21	
Abdominal Distension			
subjects affected / exposed	11 / 165 (6.67%)	13 / 169 (7.69%)	
occurrences (all)	12	14	
Proctalgia			
subjects affected / exposed	15 / 165 (9.09%)	9 / 169 (5.33%)	
occurrences (all)	15	9	
Haemorrhoids			
subjects affected / exposed	8 / 165 (4.85%)	14 / 169 (8.28%)	
occurrences (all)	8	14	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	12 / 165 (7.27%)	9 / 169 (5.33%)	
occurrences (all)	12	10	
Oral Pain			
subjects affected / exposed	7 / 165 (4.24%)	12 / 169 (7.10%)	
occurrences (all)	8	13	
Flatulence			
subjects affected / exposed	10 / 165 (6.06%)	4 / 169 (2.37%)	
occurrences (all)	10	4	
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	36 / 165 (21.82%)	43 / 169 (25.44%)	
occurrences (all)	44	55	
Pruritus			
subjects affected / exposed	33 / 165 (20.00%)	28 / 169 (16.57%)	
occurrences (all)	42	33	
Dry Skin			
subjects affected / exposed	22 / 165 (13.33%)	23 / 169 (13.61%)	
occurrences (all)	26	26	
Erythema			
subjects affected / exposed	13 / 165 (7.88%)	23 / 169 (13.61%)	
occurrences (all)	17	32	
Rash Maculo-Papular			
subjects affected / exposed	15 / 165 (9.09%)	18 / 169 (10.65%)	
occurrences (all)	20	23	
Urticaria			
subjects affected / exposed	4 / 165 (2.42%)	9 / 169 (5.33%)	
occurrences (all)	4	9	
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	20 / 165 (12.12%)	21 / 169 (12.43%)	
occurrences (all)	21	24	
Dysuria			
subjects affected / exposed	12 / 165 (7.27%)	13 / 169 (7.69%)	
occurrences (all)	13	13	
Haematuria			
subjects affected / exposed	13 / 165 (7.88%)	9 / 169 (5.33%)	
occurrences (all)	13	9	
Pollakiuria			
subjects affected / exposed	7 / 165 (4.24%)	9 / 169 (5.33%)	
occurrences (all)	8	9	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	20 / 165 (12.12%)	36 / 169 (21.30%)	
occurrences (all)	20	41	
Arthralgia			

subjects affected / exposed	19 / 165 (11.52%)	24 / 169 (14.20%)	
occurrences (all)	25	34	
Pain In Extremity			
subjects affected / exposed	16 / 165 (9.70%)	17 / 169 (10.06%)	
occurrences (all)	20	21	
Infections and infestations			
Cytomegalovirus Infection Reactivation			
subjects affected / exposed	28 / 165 (16.97%)	37 / 169 (21.89%)	
occurrences (all)	40	48	
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	52 / 165 (31.52%)	60 / 169 (35.50%)	
occurrences (all)	57	73	
Hypokalaemia			
subjects affected / exposed	54 / 165 (32.73%)	47 / 169 (27.81%)	
occurrences (all)	70	58	
Decreased Appetite			
subjects affected / exposed	40 / 165 (24.24%)	45 / 169 (26.63%)	
occurrences (all)	52	52	
Hyperglycaemia			
subjects affected / exposed	22 / 165 (13.33%)	19 / 169 (11.24%)	
occurrences (all)	35	21	
Hypocalcaemia			
subjects affected / exposed	16 / 165 (9.70%)	22 / 169 (13.02%)	
occurrences (all)	17	23	
Hypoalbuminaemia			
subjects affected / exposed	17 / 165 (10.30%)	17 / 169 (10.06%)	
occurrences (all)	18	17	
Hyponatraemia			
subjects affected / exposed	18 / 165 (10.91%)	15 / 169 (8.88%)	
occurrences (all)	21	15	
Hypophosphataemia			
subjects affected / exposed	14 / 165 (8.48%)	18 / 169 (10.65%)	
occurrences (all)	17	20	
Hyperkalaemia			

subjects affected / exposed	6 / 165 (3.64%)	12 / 169 (7.10%)	
occurrences (all)	7	12	
Hypervolaemia			
subjects affected / exposed	9 / 165 (5.45%)	7 / 169 (4.14%)	
occurrences (all)	11	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 June 2019	The following is a summary of the changes made in the amendment 06: • Consolidation of the previous local amendments to meet local regulations into a single global amendment. • Addition of final results from the completed Study Vedolizumab-1015. • Clarification of the screening window and that subjects may be rescreened. • Clarification that randomization may occur within 2 days of the first dose of study drug on Day -1. • Clarification of the inclusion and exclusion criteria. • Clarification of the excluded and permitted concomitant medications. • Addition of a criterion for withdrawal of a subject from the study for lack of efficacy. • Clarification of the management of clinical events. • Clarification regarding unscheduled PK sample collection. • Clarification regarding AEs: management of clinical events, specification of AESIs, and reporting periods for collection of AEs and SAEs. • Clarification of the timing of the primary analysis for efficacy and safety. • Clarifications to the footnotes of the schedule of events to align with updates to text.
18 September 2019	The following is a summary of the changes made in the amendment 07: 1. Clarification of the description of the disease to be treated in adolescent subjects. 2. Addition of results from nonclinical studies related to inclusion of adolescent subjects. 3. Updated human experience as reported in the 9th development safety update report. 4. Update to the study rationale to support the inclusion of adolescent subjects. 5. Update to the benefit:risk profile to support the inclusion of adolescent subjects. 6. Addition of data supporting the dose regimen in adolescent subjects. 7. Update of the inclusion criteria impacted by inclusion of adolescent subjects. 8. Update to permitted medications to include use of topical anesthetic in adolescent subjects. 9. Clarification to the procedures to be conducted after discontinuation or withdrawal of a subject. 10. Added assessment of height to be collected at the end of study visit. 11. Updated the pregnancy testing and contraception requirements to include female adolescent subjects aged 12 years and greater. 12. Addition of necessary age-appropriate documentation that must be completed for adolescent subjects. 13. Addition of blood collection volumes for adolescent and adult subjects. 14. Update to the version of Common Terminology Criteria for Adverse Events to be used for the grading of adverse events. 15. Update to stratification to include age group and data assessments in adolescent subjects. 16. Updates to Appendix A, Schedule of Events footnotes, to align with updates in text. 17. Update to Appendix B regarding methotrexate treatment to support the inclusion of adolescent subjects. 18. Update to Appendix F to include age-appropriate assessments of aGvHD clinical stage and Mount Sinai Acute GVHD International Consortium severity index for aGvHD.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported