



Clinical trial results:

A Phase III, Double-Blind, Randomized, Placebo-Controlled, Multicenter Clinical Trial to Study the Safety, Tolerability, Efficacy, and Immunogenicity of V212 in Recipients of Autologous Hematopoietic Cell Transplants (HCTs)

Summary

EudraCT number	2010-020150-34
Trial protocol	DE NL ES SE CZ GB LT IT BE PT
Global end of trial date	23 December 2015

Results information

Result version number	v1 (current)
This version publication date	04 December 2016
First version publication date	04 December 2016

Trial information

Trial identification

Sponsor protocol code	V212-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01229267
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

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	23 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 December 2015
Global end of trial reached?	Yes
Global end of trial date	23 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study to determine whether investigational V212 reduces the incidence of herpes zoster (HZ) compared to placebo when administered to recipients of autologous hematopoietic cell transplants (auto-HCT).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 16
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Belgium: 70
Country: Number of subjects enrolled	Brazil: 25
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Colombia: 34
Country: Number of subjects enrolled	Croatia: 10
Country: Number of subjects enrolled	Czech Republic: 66
Country: Number of subjects enrolled	Ecuador: 3
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Germany: 100
Country: Number of subjects enrolled	Israel: 44
Country: Number of subjects enrolled	Italy: 38
Country: Number of subjects enrolled	Korea, Republic of: 61
Country: Number of subjects enrolled	Lithuania: 20
Country: Number of subjects enrolled	Mexico: 12
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Panama: 10
Country: Number of subjects enrolled	Peru: 12

Country: Number of subjects enrolled	Portugal: 14
Country: Number of subjects enrolled	Puerto Rico: 2
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Spain: 42
Country: Number of subjects enrolled	Sweden: 16
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	United States: 540
Worldwide total number of subjects	1230
EEA total number of subjects	429

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)	982
From 65 to 84 years	248
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled men and women 18 years of age or older who were varicella history positive (or VZV antibody positive) and were scheduled to receive an auto-HCT for treatment of lymphoma or other indication (including any other malignancies) within 60 days of enrollment. Additional inclusion and exclusion criteria applied.

Pre-assignment

Screening details:

A total of 1323 participants were screened and 1257 were randomized. Twenty-seven participants were removed from all analyses due to the identification of major Good Clinical Practice compliance issues at a single site. Thus, a total of 1230 participants were enrolled in the study.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	V212 Consistency Lots (excluding High Antigen Lot)

Arm description:

V212 consistency Lot 1, 2, or 3 (Excluding High Antigen Lot) administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.

Arm type	Experimental
Investigational medicinal product name	V212
Investigational medicinal product code	
Other name	Inactivated Varicella-Zoster (VZV) vaccine Consistency Lot 1, 2, or 3
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5-mL subcutaneous injection alternating deltoid muscles for consecutive vaccinations

Arm title	V212 High Antigen Lot
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Arm description:

V212 High Antigen Lot administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.

Arm type	Experimental
Investigational medicinal product name	V212
Investigational medicinal product code	
Other name	Inactivated Varicella-Zoster (VZV) vaccine High Antigen Lot
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5-mL subcutaneous injection alternating deltoid muscles for consecutive vaccinations

Arm title	Placebo
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Arm description:

Placebo to V212 administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo to V212
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5-mL subcutaneous injection alternating deltoid muscles for consecutive vaccinations

Number of subjects in period 1	V212 Consistency Lots (excluding High Antigen Lot)	V212 High Antigen Lot	Placebo
Started	560	106	564
Received Vaccination 1	554	104	556
Received Vaccination 2	502	94	511
Received Vaccination 3	478	89	491
Received Vaccination 4	453	87	477
Completed	311	71	344
Not completed	249	35	220
Consent withdrawn by subject	77	14	59
Physician decision	27	3	25
Adverse event, non-fatal	13	2	10
Death	112	13	103
Lost to follow-up	19	3	22
Progressive disease	-	-	1
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	V212 Consistency Lots (excluding High Antigen Lot)
Reporting group description: V212 consistency Lot 1, 2, or 3 (Excluding High Antigen Lot) administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.	
Reporting group title	V212 High Antigen Lot
Reporting group description: V212 High Antigen Lot administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.	
Reporting group title	Placebo
Reporting group description: Placebo to V212 administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.	

Reporting group values	V212 Consistency Lots (excluding High Antigen Lot)	V212 High Antigen Lot	Placebo
Number of subjects	560	106	564
Age Categorical Units: Subjects			
Adults (18-64 years)	448	83	451
From 65-84 years	112	23	113
Age Continuous Units: years			
arithmetic mean	54.1	54.3	54.1
standard deviation	± 12.6	± 12.2	± 12.2
Gender Categorical Units: Subjects			
Female	203	48	204
Male	357	58	360

Reporting group values	Total		
Number of subjects	1230		
Age Categorical Units: Subjects			
Adults (18-64 years)	982		
From 65-84 years	248		
Age Continuous Units: years			
arithmetic mean	-		
standard deviation	-		
Gender Categorical Units: Subjects			
Female	455		
Male	775		

End points

End points reporting groups

Reporting group title	V212 Consistency Lots (excluding High Antigen Lot)
Reporting group description: V212 consistency Lot 1, 2, or 3 (Excluding High Antigen Lot) administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.	
Reporting group title	V212 High Antigen Lot
Reporting group description: V212 High Antigen Lot administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.	
Reporting group title	Placebo
Reporting group description: Placebo to V212 administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.	
Subject analysis set title	All V212 (including High Antigen Lot)
Subject analysis set type	Safety analysis
Subject analysis set description: V212 Consistency Lot 1, 2, 3 or High Antigen Lot administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.	
Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description: Placebo to V212 administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT. Follow-up is for up to approximately 57 months.	

Primary: Incidence of Confirmed Herpes-Zoster

End point title	Incidence of Confirmed Herpes-Zoster ^[1]
End point description: Clinical criteria for suspected HZ cases were the development of a papular or vesicular rash with a dermatomal or generalized distribution, or in the absence of a rash, clinical suspicion of VZV infection with or without the detection of VZV in diagnostic specimens from blood, cerebrospinal fluid, lung, liver, or other organ. All suspected cases of HZ were subjected to adjudication by the Clinical Adjudication Committee (CAC). Case confirmation was based on skin lesion polymerase chain reaction, if available, or by adjudication of the clinical case description by the CAC, conducted according to the CAC Standard Operations Procedure. This analysis was based on Modified Intent-to-Treat (MITT) population. The MITT population included all randomized participants who received at least one dose of vaccination and underwent auto-HCT. This endpoint did not apply to participants receiving the V212 High Antigen Lot.	
End point type	Primary
End point timeframe: Up to approximately 57 months	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint did not apply to participants receiving the V212 High Antigen lot.

End point values	V212 Consistency Lots (excluding High Antigen Lot)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	538	535		
Units: Number of cases per 1000 person years				
number (confidence interval 95%)	32.889	91.883		

(23.703 to
44.456)(75.725 to
110.469)**Statistical analyses**

Statistical analysis title	Vaccine Efficacy: Incidence of Confirmed HZ
Statistical analysis description:	
Vaccine efficacy was calculated as 1 minus the hazard ratio of HZ in the V212 (excluding High Antigen Lot) group versus the placebo group. The success criterion for vaccine efficacy required that the lower bound of the 95% CI is >0.25.	
Comparison groups	Placebo v V212 Consistency Lots (excluding High Antigen Lot)
Number of subjects included in analysis	1073
Analysis specification	Pre-specified
Analysis type	other ^[2]
Parameter estimate	Vaccine Efficacy
Point estimate	0.638
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.484
upper limit	0.746

Notes:

[2] - Point estimate and 95% Confidence Interval (CI) of vaccine efficacy were obtained from a Cox proportional hazards regression model, adjusting for age (< 50 years of age versus ≥ 50 years of age), and expected duration of antiviral prophylaxis (≤ 3 months versus 3 to 6 months after auto-HCT).

Primary: Percentage of Participants with One or More Serious Adverse Event

End point title	Percentage of Participants with One or More Serious Adverse Event		
End point description:			
An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the sponsor's product, whether or not considered related to the use of the product. A serious adverse event (SAE) is an AE that results in death, is life threatening, results in a persistent or significant disability or incapacity, results in or prolongs an existing hospitalization, is a congenital anomaly or birth defect, is a cancer, is an overdose, or is another important medical event. The analysis population included all participants who received ≥1 dose of vaccination or placebo and had safety follow-up. One participant randomized to placebo was cross-treated; this participant was excluded from the safety analyses. Safety analyses in the study were based on the pooled data from Consistency Lot 1, 2, 3 and High Antigen Lot.			
End point type	Primary		
End point timeframe:			
Up to 28 days after vaccination 4			

End point values	All V212 (including High Antigen Lot)	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	657	554		
Units: Percentage of participants				
number (not applicable)	32.9	32.7		

Statistical analyses

Statistical analysis title	Risk Difference
Statistical analysis description:	
Risk difference and 95% confidence intervals are based on Miettinen & Nurminen method stratified by age and intended duration of antiviral prophylaxis.	
Comparison groups	All V212 (including High Antigen Lot) v Placebo
Number of subjects included in analysis	1211
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	5.5

Secondary: Incidence of Moderate to Severe Herpes-Zoster-Associated Pain

End point title	Incidence of Moderate to Severe Herpes-Zoster-Associated
End point description:	
Moderate to severe HZ-associated pain was defined as 2 or more occurrences of a score 3 or greater (0-to-10 scale, where 0 is no pain and 10 is pain as bad as you can imagine) on the Zoster Brief Pain Inventory at any time from HZ onset through the end of the 6 month HZ-follow-up period. This analysis was based on Modified Intent-to-Treat (MITT) population. The MITT population included all randomized participants who received at least one dose of vaccination and underwent auto-HCT. This endpoint did not apply to participants receiving the V212 High Antigen Lot.	
End point type	Secondary
End point timeframe:	
Up to 6 months after the onset of HZ	

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint did not apply to participants receiving the V212 High Antigen lot.

End point values	V212 Consistency Lots (excluding High Antigen Lot)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	538	535		
Units: Number of cases per 1000 person years				
number (confidence interval 95%)	14.878 (8.958 to 23.234)	49.601 (37.941 to		

Statistical analyses

Statistical analysis title	Vaccine Efficacy: Incidence of HZ-associated Pain
Statistical analysis description:	
Vaccine efficacy was calculated as 1 minus the hazard ratio of HZ pain in the V212 (excluding High Antigen Lot) group versus the placebo group.	
Comparison groups	Placebo v V212 Consistency Lots (excluding High Antigen Lot)
Number of subjects included in analysis	1073
Analysis specification	Pre-specified
Analysis type	other ^[4]
Parameter estimate	Vaccine efficacy
Point estimate	0.695
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.818

Notes:

[4] - Point estimate and 95% CI of vaccine efficacy were obtained from a Cox proportional hazards regression model, adjusting for vaccination group, age (<50 years of age versus ≥50 years of age), and expected duration of antiviral prophylaxis (≤3 months versus >3 and ≤6 months after auto-HCT).

Secondary: Incidence of Herpes-Zoster Complications

End point title	Incidence of Herpes-Zoster Complications ^[5]
End point description:	
The composite efficacy endpoint of the incidence of HZ complications was defined as the occurrence of any of the following during the study: hospitalization or prolongation of hospitalization due to HZ, disseminated HZ (including disseminated HZ rash or VZV viremia), visceral HZ, ophthalmic HZ, neurological impairment due to HZ, or administration of intravenous acyclovir therapy for treatment of HZ. This analysis was based on Modified Intent-to-Treat (MITT) population. The MITT population included all randomized participants who received at least one dose of vaccination and underwent auto-HCT. This endpoint did not apply to participants receiving the V212 High Antigen Lot.	
End point type	Secondary
End point timeframe:	
Up to approximately 57 months	

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint did not apply to participants receiving the V212 High Antigen lot.

End point values	V212 Consistency Lots (excluding High Antigen Lot)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	538	535		
Units: Number of cases per 1000 person years				
number (confidence interval 95%)	9.397 (4.855)	35.77 (25.996)		

Statistical analyses

Statistical analysis title	Vaccine Efficacy: Incidence of HZ Complications
Statistical analysis description:	
Vaccine efficacy was calculated as 1 minus the hazard ratio of HZ complications in the V212 [excluding High Antigen Lot] group versus the placebo group.	
Comparison groups	Placebo v V212 Consistency Lots (excluding High Antigen Lot)
Number of subjects included in analysis	1073
Analysis specification	Pre-specified
Analysis type	other ^[6]
Parameter estimate	Vaccine efficacy
Point estimate	0.735
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.498
upper limit	0.86

Notes:

[6] - Point estimate and 95% CI of vaccine efficacy were obtained from a Cox proportional hazards regression model, adjusting for vaccination group, age (<50 years of age versus ≥50 years of age), and expected duration of antiviral prophylaxis (≤3 months versus >3 and ≤6 months after auto-HCT).

Secondary: Incidence of Postherpetic Neuralgia

End point title	Incidence of Postherpetic Neuralgia ^[7]
End point description:	
Postherpetic Neuralgia (PHN) was defined as pain in the area of the HZ rash with a pain in the last 24 hours score of 3 or greater (on a 0 to 10 scale, where 0 is no pain and 10 is pain as bad as you can imagine) on the ZBPI that persists or appears greater than or equal to 90 days after HZ rash onset. This analysis was based on Modified Intent-to-Treat (MITT) population. The MITT population included all randomized participants who received at least one dose of vaccination and underwent auto-HCT. This endpoint did not apply to participants receiving the V212 High Antigen Lot.	
End point type	Secondary
End point timeframe:	
Up to 6 months after the onset of HZ rash	

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint did not apply to participants receiving the V212 High Antigen lot.

End point values	V212 Consistency Lots (excluding High Antigen Lot)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	538	535		
Units: Number of cases per 1000 person years				
number (confidence interval 95%)	2.349 (0.484 to 6.865)	14.636 (8.674 to 23.132)		

Statistical analyses

Statistical analysis title	Vaccine Efficacy: Incidence of PHN
Statistical analysis description: Vaccine efficacy was calculated as 1 minus the hazard ratio of PHN in the V212 [excluding High Antigen Lot] group versus placebo group.	
Comparison groups	Placebo v V212 Consistency Lots (excluding High Antigen Lot)
Number of subjects included in analysis	1073
Analysis specification	Pre-specified
Analysis type	other ^[8]
Parameter estimate	Vaccine efficacy
Point estimate	0.837
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.446
upper limit	0.952

Notes:

[8] - Point estimate and 95% CI of vaccine efficacy were obtained from a Cox proportional hazards regression model, adjusting for age (<50 years of age versus ≥50 years of age), and expected duration of antiviral prophylaxis (≤3 months versus 3 to 6 months after auto-HCT).

Other pre-specified: Percentage of Participants with Study Medication Withdrawn due to an Adverse Event

End point title	Percentage of Participants with Study Medication Withdrawn due to an Adverse Event
End point description: An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the sponsor's product, whether or not considered related to the use of the product. The analysis population included all subjects who received ≥1 dose of vaccination or placebo and had safety follow-up. One participant randomized to placebo was cross-treated; this participant was excluded from the safety analyses. Safety analyses in the study were based on the pooled data from Consistency Lot 1, 2, 3 and High Antigen Lot.	
End point type	Other pre-specified
End point timeframe: Up to 28 days after vaccination 4	

End point values	All V212 (including High Antigen Lot)	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	657	554		
Units: Percentage of participants				
number (not applicable)	3	3.1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 57 months after vaccination 1

Adverse event reporting additional description:

All Subjects as Treated population included all who received ≥ 1 dose of vaccination or placebo and had safety follow-up. One participant randomized to placebo was cross-treated; this participant was excluded from the safety analyses. Safety analyses in the study were based on the pooled data from Consistency Lot 1, 2, 3 and High Antigen Lot.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	V212 [including High Antigen Lot]
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Reporting group description:

V212 Consistency Lot 1, 2, 3 or High Antigen Lot administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.

Reporting group title	Placebo
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Reporting group description:

Placebo to V212 administered by subcutaneous injection 30 days before and 30, 60, and 90 days after auto-HCT.

Serious adverse events	V212 [including High Antigen Lot]	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	420 / 657 (63.93%)	374 / 554 (67.51%)	
number of deaths (all causes)	136	107	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute myeloid leukaemia			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia recurrent			

subjects affected / exposed	0 / 657 (0.00%)	3 / 554 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Acute promyelocytic leukaemia			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma gastric			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anaplastic large cell lymphoma T- and null-cell types			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Anaplastic large cell lymphoma T- and null-cell types recurrent			
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anaplastic large-cell lymphoma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Angiocentric lymphoma			
subjects affected / exposed	0 / 657 (0.00%)	3 / 554 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioimmunoblastic T-cell lymphoma recurrent			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
B-cell lymphoma			

subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma recurrent			
subjects affected / exposed	3 / 657 (0.46%)	5 / 554 (0.90%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
B-cell lymphoma stage IV			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 657 (0.15%)	3 / 554 (0.54%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Central nervous system lymphoma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Cholangiocarcinoma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic lymphocytic leukaemia recurrent		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Chronic myeloid leukaemia		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon adenoma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer metastatic		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colorectal cancer		
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Diffuse large B-cell lymphoma		

subjects affected / exposed	10 / 657 (1.52%)	10 / 554 (1.81%)	
occurrences causally related to treatment / all	0 / 11	0 / 11	
deaths causally related to treatment / all	0 / 5	0 / 5	
Diffuse large B-cell lymphoma recurrent			
subjects affected / exposed	14 / 657 (2.13%)	10 / 554 (1.81%)	
occurrences causally related to treatment / all	0 / 14	0 / 10	
deaths causally related to treatment / all	0 / 6	0 / 6	
Diffuse large B-cell lymphoma refractory			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Extranodal marginal zone B-cell lymphoma (MALT type) recurrent			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicle centre lymphoma, follicular grade I, II, III recurrent			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	8 / 657 (1.22%)	5 / 554 (0.90%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 1	
Hodgkin's disease nodular sclerosis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease recurrent			
subjects affected / exposed	7 / 657 (1.07%)	6 / 554 (1.08%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 3	0 / 1	

Langerhans' cell histiocytosis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia recurrent			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung neoplasm malignant			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymphoma			
subjects affected / exposed	9 / 657 (1.37%)	6 / 554 (1.08%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 0	
Lymphoplasmacytoid lymphoma/immunocytoma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant lymphoid neoplasm			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma			
subjects affected / exposed	1 / 657 (0.15%)	4 / 554 (0.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mantle cell lymphoma			

subjects affected / exposed	1 / 657 (0.15%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 2
Mantle cell lymphoma recurrent		
subjects affected / exposed	10 / 657 (1.52%)	9 / 554 (1.62%)
occurrences causally related to treatment / all	0 / 10	0 / 9
deaths causally related to treatment / all	0 / 4	0 / 2
Metastases to meninges		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Myelodysplastic syndrome		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Neuroendocrine carcinoma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Non-Hodgkin's lymphoma		
subjects affected / exposed	6 / 657 (0.91%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 3	0 / 1
Non-Hodgkin's lymphoma recurrent		
subjects affected / exposed	10 / 657 (1.52%)	13 / 554 (2.35%)
occurrences causally related to treatment / all	0 / 11	0 / 13
deaths causally related to treatment / all	0 / 5	0 / 7
Non-Hodgkin's lymphoma refractory		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Nonkeratinising carcinoma of nasopharynx		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatic carcinoma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Papillary thyroid cancer		
subjects affected / exposed	1 / 657 (0.15%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Paraneoplastic syndrome		
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pericardial effusion malignant		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (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		
subjects affected / exposed	3 / 657 (0.46%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 2
Peripheral T-cell lymphoma unspecified recurrent		
subjects affected / exposed	4 / 657 (0.61%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2
Plasma cell myeloma		
subjects affected / exposed	67 / 657 (10.20%)	51 / 554 (9.21%)
occurrences causally related to treatment / all	0 / 75	0 / 57
deaths causally related to treatment / all	0 / 24	0 / 15
Plasma cell myeloma recurrent		

subjects affected / exposed	50 / 657 (7.61%)	53 / 554 (9.57%)	
occurrences causally related to treatment / all	0 / 51	0 / 56	
deaths causally related to treatment / all	0 / 13	0 / 15	
Plasmablastic lymphoma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasmacytoma			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Precursor T-lymphoblastic lymphoma/leukaemia			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Precursor T-lymphoblastic lymphoma/leukaemia recurrent			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Primary mediastinal large B-cell lymphoma			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rectal cancer			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal cancer recurrent			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell carcinoma			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	2 / 657 (0.30%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
T-cell lymphoma recurrent			
subjects affected / exposed	8 / 657 (1.22%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 0	
Tumour flare			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Aortic stenosis		
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Deep vein thrombosis		
subjects affected / exposed	7 / 657 (1.07%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Embolism		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypertension		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypertensive crisis		
subjects affected / exposed	0 / 657 (0.00%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Hypotension		
subjects affected / exposed	5 / 657 (0.76%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Orthostatic hypotension		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral arterial occlusive disease		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venoocclusive disease			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Threatened labour			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	4 / 657 (0.61%)	3 / 554 (0.54%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	5 / 657 (0.76%)	4 / 554 (0.72%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 5	0 / 4	

Drug withdrawal syndrome			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	8 / 657 (1.22%)	6 / 554 (1.08%)	
occurrences causally related to treatment / all	0 / 8	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	3 / 657 (0.46%)	3 / 554 (0.54%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 3	
Pneumatosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	33 / 657 (5.02%)	26 / 554 (4.69%)	
occurrences causally related to treatment / all	0 / 37	1 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			

subjects affected / exposed	2 / 657 (0.30%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcer haemorrhage			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Acute graft versus host disease in skin			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyloidosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Engraftment syndrome			
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease			

subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (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 liver			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Graft versus host disease in lung			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (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 skin			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Primary amyloidosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired phimosis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 657 (0.46%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pneumonia syndrome			

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
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	2 / 657 (0.30%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung consolidation			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumomediastinum			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
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 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia aspiration		
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonitis		
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)
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 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary embolism		
subjects affected / exposed	6 / 657 (0.91%)	5 / 554 (0.90%)
occurrences causally related to treatment / all	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary hypertension		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary mass		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pulmonary oedema		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Respiratory distress		

subjects affected / exposed	3 / 657 (0.46%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 657 (0.46%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Restrictive pulmonary disease			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomania			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Schizoaffective disorder			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compression fracture			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delayed engraftment			
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 657 (0.15%)	3 / 554 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve injury			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypotension			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant dysfunction			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	5 / 657 (0.76%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0
Arrhythmia		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Atrial fibrillation		
subjects affected / exposed	4 / 657 (0.61%)	5 / 554 (0.90%)
occurrences causally related to treatment / all	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 0
Atrial flutter		
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bradycardia		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac amyloidosis		
subjects affected / exposed	0 / 657 (0.00%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 3
Cardiac failure		
subjects affected / exposed	3 / 657 (0.46%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure acute		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure chronic		

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	5 / 657 (0.76%)	5 / 554 (0.90%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cardiac ventricular thrombosis			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery disease			
subjects affected / exposed	2 / 657 (0.30%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			

subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery aneurysm			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery disease			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	4 / 657 (0.61%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Facial paralysis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Headache		
subjects affected / exposed	2 / 657 (0.30%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic encephalopathy		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypoglycaemic coma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intracranial venous sinus thrombosis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Metabolic encephalopathy		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Migraine		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Paraesthesia		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	6 / 657 (0.91%)	5 / 554 (0.90%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Abdominal lymphadenopathy			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired haemophilia			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Agranulocytosis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	3 / 657 (0.46%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1
Anaemia megaloblastic		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bone marrow failure		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Febrile neutropenia		
subjects affected / exposed	42 / 657 (6.39%)	38 / 554 (6.86%)
occurrences causally related to treatment / all	0 / 44	0 / 47
deaths causally related to treatment / all	0 / 0	0 / 0
Heparin-induced thrombocytopenia		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Immune thrombocytopenic purpura		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Leukocytosis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lymphadenopathy		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Methaemoglobinaemia		

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	4 / 657 (0.61%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	1 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sickle cell anaemia with crisis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infarction			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	8 / 657 (1.22%)	7 / 554 (1.26%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular haematoma			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal incontinence			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphthous ulcer			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	7 / 657 (1.07%)	15 / 554 (2.71%)	
occurrences causally related to treatment / all	0 / 7	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyskinesia oesophageal			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric ulcer haemorrhage		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastritis		
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal disorder		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal haemorrhage		
subjects affected / exposed	1 / 657 (0.15%)	5 / 554 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal obstruction		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Haematemesis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haematochezia		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haemorrhoids		

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ileus		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Impaired gastric emptying		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Inguinal hernia		
subjects affected / exposed	3 / 657 (0.46%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal infarction		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Intestinal ischaemia		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal obstruction		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Intra-abdominal haematoma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Large intestine perforation		

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Large intestine polyp		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lower gastrointestinal haemorrhage		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Mesenteritis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nausea		
subjects affected / exposed	3 / 657 (0.46%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Neutropenic colitis		
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatic insufficiency		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatitis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatitis acute		

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	4 / 657 (0.61%)	5 / 554 (0.90%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cholangitis acute		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cholecystitis		
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cholecystitis acute		
subjects affected / exposed	2 / 657 (0.30%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cholelithiasis obstructive		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Granulomatous liver disease		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic cirrhosis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Hepatic failure		
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Hydrocholecystitis		

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal hypertension			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis exfoliative			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash vesicular			
subjects affected / exposed	3 / 657 (0.46%)	3 / 554 (0.54%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	8 / 657 (1.22%)	10 / 554 (1.81%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute prerenal failure			
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	4 / 657 (0.61%)	5 / 554 (0.90%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal injury			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (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	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudarthrosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Actinomycotic pulmonary infection			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Anal abscess		
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Appendicitis		
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Appendicitis perforated		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Arthritis bacterial		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Aspergilloma		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Aspergillus infection		
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
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	6 / 657 (0.91%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0
BK virus infection		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bacteraemia		
subjects affected / exposed	4 / 657 (0.61%)	7 / 554 (1.26%)
occurrences causally related to treatment / all	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 1	0 / 0
Bacterial sepsis		
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchiolitis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchitis		
subjects affected / exposed	4 / 657 (0.61%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchitis bacterial		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchitis viral		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchopulmonary aspergillosis		
subjects affected / exposed	6 / 657 (0.91%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1
Candida sepsis		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cellulitis		
subjects affected / exposed	4 / 657 (0.61%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Cholangitis infective		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic hepatitis B		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Clostridial infection		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Clostridium colitis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Clostridium difficile colitis		
subjects affected / exposed	5 / 657 (0.76%)	5 / 554 (0.90%)
occurrences causally related to treatment / all	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Clostridium difficile infection		
subjects affected / exposed	3 / 657 (0.46%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Coxsackie viral infection		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cystitis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cytomegalovirus colitis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Cytomegalovirus infection		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cytomegalovirus oesophagitis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dengue fever		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Device related infection		
subjects affected / exposed	5 / 657 (0.76%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Device related sepsis		
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulitis		

subjects affected / exposed	3 / 657 (0.46%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Empyema		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enterococcal bacteraemia		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enterococcal infection		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enterocolitis bacterial		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enterovirus infection		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Epididymitis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Erysipelas		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia bacteraemia		

subjects affected / exposed	2 / 657 (0.30%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	3 / 657 (0.46%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal oesophagitis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (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	5 / 657 (0.76%)	4 / 554 (0.72%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal candidiasis			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal infection		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Groin abscess		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
H1N1 influenza		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haemophilus infection		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes zoster		
subjects affected / exposed	3 / 657 (0.46%)	12 / 554 (2.17%)
occurrences causally related to treatment / all	0 / 3	0 / 12
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes zoster disseminated		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infected lymphocele		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infection		

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infection in an immunocompromised host		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Influenza		
subjects affected / exposed	8 / 657 (1.22%)	7 / 554 (1.26%)
occurrences causally related to treatment / all	0 / 8	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
Klebsiella bacteraemia		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Klebsiella infection		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lower respiratory tract infection		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lower respiratory tract infection viral		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lung abscess		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lung infection		
subjects affected / exposed	3 / 657 (0.46%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Lung infection pseudomonal		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Meningitis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Meningitis pneumococcal		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Meningoencephalitis herpetic		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nasopharyngitis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (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	3 / 657 (0.46%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 1
Oral candidiasis		

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Parainfluenzae virus infection		
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pharyngitis		
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumococcal bacteraemia		
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumococcal sepsis		
subjects affected / exposed	1 / 657 (0.15%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1
Pneumocystis jirovecii infection		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia		
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Pneumonia		
subjects affected / exposed	61 / 657 (9.28%)	56 / 554 (10.11%)
occurrences causally related to treatment / all	0 / 74	1 / 67
deaths causally related to treatment / all	0 / 5	0 / 6
Pneumonia bacterial		

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			

subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal bacteraemia			
subjects affected / exposed	2 / 657 (0.30%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pseudomonas infection			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mycosis			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Respiratory tract infection viral		
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Retinitis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
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	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Scrotal abscess		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sepsis		
subjects affected / exposed	19 / 657 (2.89%)	12 / 554 (2.17%)
occurrences causally related to treatment / all	0 / 19	0 / 14
deaths causally related to treatment / all	0 / 5	0 / 3
Sepsis syndrome		
subjects affected / exposed	1 / 657 (0.15%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Septic shock		
subjects affected / exposed	7 / 657 (1.07%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 6	0 / 3
Sialoadenitis		

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sinusitis		
subjects affected / exposed	1 / 657 (0.15%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal bacteraemia		
subjects affected / exposed	4 / 657 (0.61%)	3 / 554 (0.54%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal infection		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal sepsis		
subjects affected / exposed	2 / 657 (0.30%)	4 / 554 (0.72%)
occurrences causally related to treatment / all	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Streptococcal bacteraemia		
subjects affected / exposed	1 / 657 (0.15%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Streptococcal sepsis		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
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	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Thrombophlebitis septic		

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tooth abscess		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tuberculosis		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Upper respiratory tract infection		
subjects affected / exposed	5 / 657 (0.76%)	5 / 554 (0.90%)
occurrences causally related to treatment / all	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Urinary tract infection		
subjects affected / exposed	8 / 657 (1.22%)	5 / 554 (0.90%)
occurrences causally related to treatment / all	0 / 10	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Urosepsis		
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Varicella		
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Varicella zoster virus infection		
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Viral infection		

subjects affected / exposed	2 / 657 (0.30%)	5 / 554 (0.90%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral sepsis			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection bacterial			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	2 / 657 (0.30%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	3 / 657 (0.46%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Food intolerance			

subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	2 / 657 (0.30%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 657 (0.00%)	2 / 554 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactose intolerance			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tetany			
subjects affected / exposed	0 / 657 (0.00%)	1 / 554 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			

subjects affected / exposed	1 / 657 (0.15%)	0 / 554 (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: 5 %

Non-serious adverse events	V212 [including High Antigen Lot]	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	625 / 657 (95.13%)	512 / 554 (92.42%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	33 / 657 (5.02%)	33 / 554 (5.96%)	
occurrences (all)	38	36	
Hypotension			
subjects affected / exposed	57 / 657 (8.68%)	48 / 554 (8.66%)	
occurrences (all)	64	52	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	45 / 657 (6.85%)	34 / 554 (6.14%)	
occurrences (all)	47	35	
Nervous system disorders			
Dizziness			
subjects affected / exposed	44 / 657 (6.70%)	46 / 554 (8.30%)	
occurrences (all)	46	51	
Dysgeusia			
subjects affected / exposed	29 / 657 (4.41%)	28 / 554 (5.05%)	
occurrences (all)	29	28	
Headache			
subjects affected / exposed	131 / 657 (19.94%)	114 / 554 (20.58%)	
occurrences (all)	149	141	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	175 / 657 (26.64%)	134 / 554 (24.19%)	
occurrences (all)	201	168	
Febrile neutropenia			

subjects affected / exposed	184 / 657 (28.01%)	135 / 554 (24.37%)
occurrences (all)	191	138
Leukopenia		
subjects affected / exposed	33 / 657 (5.02%)	32 / 554 (5.78%)
occurrences (all)	34	41
Neutropenia		
subjects affected / exposed	163 / 657 (24.81%)	129 / 554 (23.29%)
occurrences (all)	187	157
Pancytopenia		
subjects affected / exposed	63 / 657 (9.59%)	53 / 554 (9.57%)
occurrences (all)	64	54
Thrombocytopenia		
subjects affected / exposed	238 / 657 (36.23%)	212 / 554 (38.27%)
occurrences (all)	289	264
General disorders and administration site conditions		
Asthenia		
subjects affected / exposed	72 / 657 (10.96%)	60 / 554 (10.83%)
occurrences (all)	77	68
Chills		
subjects affected / exposed	39 / 657 (5.94%)	35 / 554 (6.32%)
occurrences (all)	44	42
Fatigue		
subjects affected / exposed	144 / 657 (21.92%)	121 / 554 (21.84%)
occurrences (all)	159	131
Injection site erythema		
subjects affected / exposed	153 / 657 (23.29%)	14 / 554 (2.53%)
occurrences (all)	323	19
Injection site pain		
subjects affected / exposed	133 / 657 (20.24%)	21 / 554 (3.79%)
occurrences (all)	283	24
Injection site pruritus		
subjects affected / exposed	35 / 657 (5.33%)	4 / 554 (0.72%)
occurrences (all)	52	5
Injection site swelling		

subjects affected / exposed	124 / 657 (18.87%)	9 / 554 (1.62%)
occurrences (all)	257	9
Mucosal inflammation		
subjects affected / exposed	254 / 657 (38.66%)	226 / 554 (40.79%)
occurrences (all)	271	244
Oedema peripheral		
subjects affected / exposed	77 / 657 (11.72%)	65 / 554 (11.73%)
occurrences (all)	89	72
Pyrexia		
subjects affected / exposed	317 / 657 (48.25%)	248 / 554 (44.77%)
occurrences (all)	526	374
Gastrointestinal disorders		
Abdominal pain		
subjects affected / exposed	87 / 657 (13.24%)	78 / 554 (14.08%)
occurrences (all)	103	81
Abdominal pain upper		
subjects affected / exposed	51 / 657 (7.76%)	34 / 554 (6.14%)
occurrences (all)	51	35
Constipation		
subjects affected / exposed	107 / 657 (16.29%)	102 / 554 (18.41%)
occurrences (all)	120	113
Diarrhoea		
subjects affected / exposed	394 / 657 (59.97%)	341 / 554 (61.55%)
occurrences (all)	492	396
Dyspepsia		
subjects affected / exposed	61 / 657 (9.28%)	47 / 554 (8.48%)
occurrences (all)	65	52
Nausea		
subjects affected / exposed	370 / 657 (56.32%)	319 / 554 (57.58%)
occurrences (all)	452	391
Stomatitis		
subjects affected / exposed	83 / 657 (12.63%)	51 / 554 (9.21%)
occurrences (all)	94	56
Vomiting		
subjects affected / exposed	211 / 657 (32.12%)	200 / 554 (36.10%)
occurrences (all)	265	260

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	76 / 657 (11.57%)	80 / 554 (14.44%)	
occurrences (all)	84	93	
Dyspnoea			
subjects affected / exposed	55 / 657 (8.37%)	36 / 554 (6.50%)	
occurrences (all)	60	36	
Epistaxis			
subjects affected / exposed	41 / 657 (6.24%)	24 / 554 (4.33%)	
occurrences (all)	48	26	
Oropharyngeal pain			
subjects affected / exposed	68 / 657 (10.35%)	43 / 554 (7.76%)	
occurrences (all)	78	48	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	33 / 657 (5.02%)	22 / 554 (3.97%)	
occurrences (all)	37	31	
Pruritus			
subjects affected / exposed	66 / 657 (10.05%)	38 / 554 (6.86%)	
occurrences (all)	72	45	
Rash			
subjects affected / exposed	89 / 657 (13.55%)	74 / 554 (13.36%)	
occurrences (all)	110	84	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	35 / 657 (5.33%)	31 / 554 (5.60%)	
occurrences (all)	38	32	
Insomnia			
subjects affected / exposed	84 / 657 (12.79%)	68 / 554 (12.27%)	
occurrences (all)	91	71	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	56 / 657 (8.52%)	46 / 554 (8.30%)	
occurrences (all)	63	51	
Pain in extremity			

subjects affected / exposed occurrences (all)	33 / 657 (5.02%) 35	24 / 554 (4.33%) 26	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	152 / 657 (23.14%)	132 / 554 (23.83%)	
occurrences (all)	161	150	
Hyperglycaemia			
subjects affected / exposed	33 / 657 (5.02%)	16 / 554 (2.89%)	
occurrences (all)	40	16	
Hypocalcaemia			
subjects affected / exposed	55 / 657 (8.37%)	40 / 554 (7.22%)	
occurrences (all)	65	45	
Hypokalaemia			
subjects affected / exposed	141 / 657 (21.46%)	111 / 554 (20.04%)	
occurrences (all)	165	135	
Hypomagnesaemia			
subjects affected / exposed	76 / 657 (11.57%)	62 / 554 (11.19%)	
occurrences (all)	88	75	
Hypophosphataemia			
subjects affected / exposed	41 / 657 (6.24%)	40 / 554 (7.22%)	
occurrences (all)	48	42	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2010	Amendment 1: The primary reasons for this amendment are to change the pre-specified criteria for success for the primary efficacy hypothesis and to elevate critical exploratory efficacy endpoints to secondary efficacy endpoints.
13 October 2010	Amendment 2: The primary clinical efficacy endpoint was modified to exclude recipients of inactivated VZV vaccine High Antigen Lot. Therefore, the primary clinical efficacy endpoint included the incidence of HZ among the inactivated VZV Consistency Lot 1, 2, 3 and placebo recipients only.
02 January 2013	Amendment 4: The following text was added, anticipating that an original vaccine lot might expire prior to all participants completing their 4-dose regimen: A given participant is anticipated to receive all 4 doses in the series from the same lot. In the event that the vaccine lot expires prior to a participant receiving all 4 doses of study vaccine, doses will be administered from a new lot of comparable antigen content.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 September 2012	The Data Monitoring Committee temporarily paused enrollment and vaccination to evaluate preliminary reports of disseminated rash lesions that tested PCR positive for VZV Oka/Merck (vaccine strain) in another V212 study. The available evidence suggested that these PCR results were likely false positive.	02 October 2012

Notes:

Limitations and caveats

None reported