Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial to Evaluate the Protective Efficacy and Safety of a Therapeutic Vaccine, ASP0113, in Cytomegalovirus (CMV)-Seropositive Recipients Undergoing Allogeneic, Hematopoietic Cell Transplant (HCT)

Summary

EudraCT number	2013-000903-18
Trial protocol	SE DE BE ES
Global end of trial date	01 March 2022

Results information

Result version number	v2 (current)
This version publication date	27 October 2022
First version publication date	03 October 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	0113-CL-1004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01877655
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Global Development US
Sponsor organisation address	1 Astellas Way, Northbrook, United States,
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Development US, 001 800-888-7704 ex 5473, astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Development US, 001 800-888-7704 ex 5473, astellas.resultsdisclosure@astellas.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	Interim
Date of interim/final analysis	28 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 September 2017
Global end of trial reached?	Yes
Global end of trial date	01 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate efficacy of ASP0113 compared with placebo as measured by a primary composite endpoint of overall mortality and cytomegalovirus end organ disease (CMV EOD) through 1 year posttransplant and to evaluate safety of ASP0113 in participants undergoing allogeneic hematopoietic cell transplant (HCT).

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy:

All concomitant medications and therapies administered from 30 days prior to transplant through 30 days after the last dose of study drug were recorded on the eCRF. From 31 days after the last dose of study drug through 1 year posttransplant, concomitant medications and therapies associated with all events required adjudication.

Evidence for comparator: -

Actual start date of recruitment	11 September 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	54 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Belgium: 47
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 54
Country: Number of subjects enrolled	Japan: 47
Country: Number of subjects enrolled	Korea, Republic of: 23
Country: Number of subjects enrolled	Spain: 75
Country: Number of subjects enrolled	Sweden: 31
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	United States: 170

Worldwide total number of subjects	514
EEA total number of subjects	237

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)	431
From 65 to 84 years	83
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 514 participants were enrolled across 11 countries. At least 30% of enrolled participants had CMV seronegative donor and underwent allogeneic HCT. After primary study period (day 365) 326 participants entered the long-term follow-up period and were monitored for 5.5 years post-transplant for long-term safety.

Pre-assignment

Screening details:

Screening assessment occurred from 30 to 5 days before transplant. Participants who met the inclusion and none of the exclusion criteria were randomly assigned in a 1:1 ratio to receive either ASP0113 or placebo. The randomization to treatment was stratified by donor-recipient relatedness and by donor CMV serostatus.

Period 1

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

Blinding implementation details:

Study drug assignment was blinded to all site staff except the pharmacist, designated staff and the unblinded administrator.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received 1 mL of 5 mg/mL of matching placebo via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received matching placebo in 2-mL vials containing phosphate-buffered saline.

Arm title	ASP0113 5mg

Arm description:

Participants received 1 mL of 5 mg/mL of ASP0113 via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).

Arm type	Experimental
Investigational medicinal product name	ASP0113
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received ASP0113 in single-dose 2-mL vials containing 1.3 mL of 5 mg/mL ASP0113.

Number of subjects in period 1	Placebo	ASP0113 5mg
Started	263	251
Received Treatment	255	246
Completed	165	154
Not completed	98	97
Consent withdrawn by subject	18	26
Physician decision	11	10
Death	57	52
Miscellaneous	4	4
Randomized but Never Received Drug	8	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received 1 mL of 5 mg/mL of matching placebo via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).	
Reporting group title	ASP0113 5mg
Reporting group description:	
Participants received 1 mL of 5 mg/mL of ASP0113 via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).	

Reporting group values	Placebo	ASP0113 5mg	Total
Number of subjects	263	251	514
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	52.0	51.8	
standard deviation	± 13.15	± 12.41	-
Gender categorical Units: Subjects			
Female	105	110	215
Male	158	141	299
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	47	50	97
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	7	13
White	189	177	366
More than one race	0	0	0
Unknown or Not Reported	21	17	38
Strata Units: Subjects			
Related Seropositive Donor	65	73	138
Related Seronegative Donor	30	26	56
Non-related Seropositive Donor	96	73	169
Non-related Seronegative Donor	72	79	151
Primary Diagnosis Units: Subjects			
Acute Myeloid Leukemia (AML)	126	97	223
Acute Lymphoblastic Leukemia (ALL)	34	34	68
Acute Undifferentiated Leukemia (AUL)	1	2	3
Acute Biphenotypic Leukemia (ABL)	2	2	4

Chronic Myelogenous Leukemia (CML)	6	12	18
Chronic Lymphocytic Leukemia (CLL)	7	10	17
Myelodysplastic Syndrome	46	51	97
Primary or Secondary Myelofibrosis	8	11	19
Lymphoma	33	31	64
Missing	0	1	1
Conditioning Regimen Units: Subjects			
Myeloablative	122	120	242
Non-Myeloablative	131	124	255
Missing	10	7	17
Antithymocyte Globulin (ATG) Use Units: Subjects			
ATG Use Yes	45	43	88
ATG Use No	218	208	426
Ethnicity Units: Subjects			
Hispanic or Latino	11	19	30
Not Hispanic or Latino	252	232	484
Height Units: Centimeteres			
arithmetic mean	170.6	169.7	
standard deviation	± 9.91	± 9.88	-
Body Mass Index (BMI) Units: kg/m^2			
arithmetic mean	27.0	26.0	
standard deviation	± 5.02	± 5.05	-

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received 1 mL of 5 mg/mL of matching placebo via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).

Reporting group title	ASP0113 5mg

Reporting group description:

Participants received 1 mL of 5 mg/mL of ASP0113 via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).

Primary: Percentage of Participants With Composite of All-Cause Mortality and Adjudicated Cytomegalovirus End Organ Disease (CMV EOD) Through 1 Year Post Transplant

End point title	Percentage of Participants With Composite of All-Cause Mortality and Adjudicated Cytomegalovirus End Organ Disease (CMV EOD) Through 1 Year Post Transplant

End point description:

This was the composite of all-cause mortality and adjudicated CMV EOD through 1 year posttransplant, The CMV EOD was assessed by the independent and blinded adjudication committee, which counted events that were observed up to day 380 from transplantation. Deaths that occurred up to day 365 from transplant were also counted.

End point type	Primary

End point timeframe:

From first study dose injection (Day -14 to -3 prior to transplant) up to one year post study drug injection (Day 365)

End point values	Placebo	ASP0113 5mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	246		
Units: Percentage of Participants				
number (not applicable)				
Participants With Composite Endpoint	30.20	35.37		
All-Cause Mortality	28.24	31.71		
Adjudicated CMV EOD	3.53	6.10		

Statistical analyses

Statistical analysis title	All-Cause Mortality and Adjudicated CMV EOD

Statistical analysis description:

Analysis was completed using the Cochran-Mantel-Haenszel (CMH) test at the 1-sided 5% level stratified by use of antithymocyte globulin (ATG) and by receipt of a kidney from a living or deceased donor.

Comparison groups	Placebo v ASP0113 5mg

Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.205 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.85

Notes:

[1] - P-value based on CMH general association test stratified by donor-recipient relatedness and donor CMV serostatus.

Secondary: Percentage of Participants With Protocol-Defined CMV Viremia Through 1 Year Posttransplant

End point title	Percentage of Participants With Protocol-Defined CMV Viremia Through 1 Year Posttransplant

End point description:

Protocol-defined CMV viremia was defined as a CMV plasma viral load ≥1000 IU/mL as assessed by the central laboratory. Rate was based on cumulative incidence function estimated at 1 year. The central laboratory had the lower limit of quantification [LLOQ] for CMV viral load assessment, so when the viral load was below the LLOQ the actual viral load reading was not possible and was denoted as ≤LLOQ. If participant had any CMV viral load assessments greater than the LLOQ it was classified as viremic.

End point type	Secondary

End point timeframe:

From first study dose injection (Day -14 to -3 prior to transplant) up to one year post study drug injection (Day 365)

End point values	Placebo	ASP0113 5mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	246		
Units: Percentage of Participants				
number (confidence interval 95%)	58.6 (52.0 to 64.6)	56.7 (50.1 to 62.8)		

Statistical analyses

Statistical analysis title	CMV Viremia Through 1 Yr Posttransplant

Statistical analysis description:

CMV viremia was defined by the protocol as CMV plasma viral load ≥ 1000 IU/mL as assessed by the central laboratory. The 95% CI was based on cumulative incidence function CMV viremia rate at 1 year.

Comparison groups	Placebo v ASP0113 5mg

Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.748 [2]
Method	Cox Proportional Hazard Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.22

Notes:

[2] - P-value based on cox proportional hazard model (ASP0113 v placebo) with treatment & randomization strata adjusted for death as a competing risk.

Secondary: Percentage of Participants With Adjudicated CMV-Specific Antiviral Therapy (AVT) Through 1 Year Posttransplant

End point title	Percentage of Participants With Adjudicated CMV-Specific Antiviral Therapy (AVT) Through 1 Year Posttransplant

End point description:

The CMV-specific AVT use was adjudicated by the independent and blinded committee. When the CMV-specific AVT was initiated, a central CMV viral load was obtained weekly until it was discontinued. Participants without any CMV-specific AVT events were censored on the last study evaluation.

End point type	Secondary

End point timeframe:

From first study dose injection (Day -14 to -3 prior to transplant) up to one year post study drug injection (Day 365)

End point values	Placebo	ASP0113 5mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	246		
Units: Percentage of Participants				
number (confidence interval 95%)	53.2 (46.8 to 59.1)	54.6 (48.1 to 60.6)		

Statistical analyses

Statistical analysis title	CMV-Specific Antiviral Therapy (AVT) Through 1 Yr

Statistical analysis description:

Time to first adjudicated CMV-specific therapy was defined as time to the start of AVT for CMV viremia. CMV-specific AVT was determined by the adjudication committee.

Comparison groups	Placebo v ASP0113 5mg

Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.888 [3]
Method	Cox Proportional Hazard Model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.29

Notes:

[3] - P-value based on cox proportional hazard model (ASP0113 v placebo) with treatment & randomization strata adjusted for death as a competing risk.

Secondary: Percentage of Participants With a Composite Endpoint of Protocol-defined CMV Viremia and Adjudicated CMV-Specific AVT Use

End point title	Percentage of Participants With a Composite Endpoint of Protocol-defined CMV Viremia and Adjudicated CMV-Specific AVT Use

End point description:

Protocol-defined CMV Viremia was as CMV plasma viral load ≥ 1000 IU/mL as assessed by the central laboratory. The CMV-specific AVT was determined by the adjudication committee. Participants with no posttransplant viral load data were excluded from the analysis.

End point type	Secondary

End point timeframe:

From first study dose injection (Day -14 to -3 prior to transplant) up to one year post study drug injection (Day 365)

End point values	Placebo	ASP0113 5mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	246		
Units: Percentage of Participants				
number (not applicable)	60.78	60.98		

Statistical analyses

Statistical analysis title	Composite of CMV Viremia and Adjudicated CMV-AVT

Statistical analysis description:

CMV viremia was defined by the protocol as CMV plasma viral load ≥ 1000 IU/mL as assessed by the central laboratory. CMV-specific AVT was determined by the adjudication committee. Patients with no posttransplant viral load data were excluded from the analysis.

Comparison groups	Placebo v ASP0113 5mg

Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.802 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.51

Notes:

[4] - P-value based on CMH general association test stratified by donor-recipient relatedness and donor CMV serostatus.

Secondary: Percentage of Participants With First Occurrence of Adjudicated CMV-specific AVT or Adjudicated Diagnosis of CMV EOD After Study Drug First Injection Through 1 Year Posttransplant

End point title	Percentage of Participants With First Occurrence of Adjudicated CMV-specific AVT or Adjudicated Diagnosis of CMV EOD After Study Drug First Injection Through 1 Year Posttransplant

End point description:

Rate was based on cumulative incidence function estimate at 1 year. Time to first CMV-specific AVT was defined as time to the start of AVT for CMV viremia or CMV EOD. CMV-specific AVT and EOD were determined by the adjudication committee. This endpoint was a composite endpoint based on the independent adjudication committee assessments of CMV-specific AVT and CMV EOD.

End point type	Secondary

End point timeframe:

From first study dose injection (Day -14 to -3 prior to transplant) up to one year post study drug injection (Day 365)

End point values	Placebo	ASP0113 5mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	246		
Units: Percentage of Participants				
number (confidence interval 95%)	54.4 (48.0 to 60.3)	55.4 (48.9 to 61.5)		

Statistical analyses

Statistical analysis title	Rate of Adjudicated CMV AVT or CMV EOD

Statistical analysis description:

Time to first CMV-specific AVT defined as time to the start of AVT for CMV viremia or CMV EOD. CMV-specific AVT and EOD were determined by the adjudication committee. Rate based on cumulative incidence function estimate at 1 year.

Comparison groups	Placebo v ASP0113 5mg

Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.928 [5]
Method	Cox Proportional Hazard Model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.28

Notes:

[5] - P-value based on cox proportional hazard model (ASP0113 v placebo) with treatment & randomization strata adjusted for death as a competing risk.

Secondary: All-Cause Mortality at 1 Year Posttransplant

End point title	All-Cause Mortality at 1 Year Posttransplant

End point description:

All-cause mortality through 1-year post-transplantation summary included all deaths and unknown survival status. For the known deaths, the adjudication committee assessed results and summarized them according to the following category: Mortality due to the participant's primary disease, and Mortality due to causes unrelated to the participant's primary disease. Participants with unknown survival status at 1 year were considered dead for this analysis.

End point type	Secondary

End point timeframe:

From first study dose injection (Day -14 to -3 prior to transplant) up to one year post study drug injection (Day 365)

End point values	Placebo	ASP0113 5mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	246		
Units: Percentage of Participants				
number (not applicable)	28.24	31.71		

Statistical analyses

Statistical analysis title	All-Cause Mortality at 1 Year

Statistical analysis description:

Participants with unknown survival status at 1 year were considered dead for this analysis.

Comparison groups	Placebo v ASP0113 5mg
Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.393 [6]
Method	Cox Proportional Hazards Model
Parameter estimate	Odds ratio (OR)
Point estimate	1.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.73

Notes:

[6] - P-value based on cox proportional hazards model parameter estimate for the treatment effect.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Number of Deaths: Baseline up to 5.5 years post transplant.
Adverse Events: From first dose of study drug up to 30 days after last dose of study drug (Day 365).

Adverse event reporting additional description:

TEAE was defined as an AE observed after the first dose of study drug injection through Day 365 and within 30 days of the last dose of study drug. Drug-related TEAE was defined as any TEAE with possible relationship to study treatment as assessed by the investigator. AE data was not planned to be collected during the long-term follow-up period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	ASP0113 5mg

Reporting group description:

Participants received 1 mL of 5 mg/mL of ASP0113 via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).

Reporting group title	Placebo

Reporting group description:

Participants received 1 mL of 5 mg/mL of matching placebo via intramuscular injection in the deltoid muscle alternating sides with each dose on days -14 to -3 pretransplant, 14 to 40, 60, 90 and 180 in relation to the day of transplant (Day 0).

Serious adverse events	ASP0113 5mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	221 / 246 (89.84%)	221 / 255 (86.67%)	
number of deaths (all causes)	105	100	
number of deaths resulting from adverse events	61	63	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	5 / 246 (2.03%)	6 / 255 (2.35%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	6 / 246 (2.44%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Acute lymphocytic leukaemia			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia recurrent			
subjects affected / exposed	17 / 246 (6.91%)	18 / 255 (7.06%)	
occurrences causally related to treatment / all	2 / 22	0 / 21	
deaths causally related to treatment / all	1 / 10	0 / 8	
Central nervous system lymphoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adult T-cell lymphoma/leukaemia recurrent			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia recurrent			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chloroma			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myelomonocytic leukaemia			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
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	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Leukaemia recurrent			
subjects affected / exposed	3 / 246 (1.22%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hodgkin's disease			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Kaposi's sarcoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymphoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant melanoma			

subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemic infiltration brain			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoclonal gammopathy			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Mycosis fungoides recurrent			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	5 / 246 (2.03%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	1 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral T-cell lymphoma unspecified recurrent			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma recurrent			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelofibrosis			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
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	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post transplant lymphoproliferative disorder			
subjects affected / exposed	2 / 246 (0.81%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
T-cell lymphoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma recurrent			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
T-cell type acute leukaemia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	2 / 246 (0.81%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microangiopathy			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Venous thrombosis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Appendicectomy			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central venous catheter removal			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colectomy			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug therapy			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Donor leukocyte infusion			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stem cell transplant			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral prostatectomy			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 246 (1.63%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	3 / 246 (1.22%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug resistance			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion site extravasation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			

subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	6 / 246 (2.44%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 5	0 / 2	
Oedema due to cardiac disease			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Serositis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	26 / 246 (10.57%)	23 / 255 (9.02%)	
occurrences causally related to treatment / all	2 / 27	0 / 29	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	7 / 246 (2.85%)	9 / 255 (3.53%)	
occurrences causally related to treatment / all	0 / 7	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute graft versus host disease in intestine			

subjects affected / exposed	76 / 246 (30.89%)	76 / 255 (29.80%)	
occurrences causally related to treatment / all	1 / 123	0 / 120	
deaths causally related to treatment / all	1 / 3	0 / 8	
Acute graft versus host disease in liver			
subjects affected / exposed	18 / 246 (7.32%)	24 / 255 (9.41%)	
occurrences causally related to treatment / all	1 / 23	0 / 30	
deaths causally related to treatment / all	1 / 2	0 / 3	
Acute graft versus host disease in skin			
subjects affected / exposed	118 / 246 (47.97%)	122 / 255 (47.84%)	
occurrences causally related to treatment / all	3 / 165	1 / 171	
deaths causally related to treatment / all	0 / 0	0 / 3	
Alloimmunisation			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease			
subjects affected / exposed	2 / 246 (0.81%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in intestine			
subjects affected / exposed	3 / 246 (1.22%)	6 / 255 (2.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic graft versus host disease in skin			
subjects affected / exposed	1 / 246 (0.41%)	5 / 255 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in liver			
subjects affected / exposed	3 / 246 (1.22%)	7 / 255 (2.75%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	

Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 246 (0.00%)	6 / 255 (2.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 6	
deaths causally related to treatment / all	0 / 0	1 / 5	
Acute respiratory failure			
subjects affected / exposed	2 / 246 (0.81%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Atelectasis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 246 (1.22%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemoptysis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	3 / 246 (1.22%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Idiopathic pneumonia syndrome			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	3 / 246 (1.22%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mediastinal mass			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obliterative bronchiolitis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			

subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 246 (0.41%)	7 / 255 (2.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary embolism			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary oedema			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary thrombosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			

subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	8 / 246 (3.25%)	11 / 255 (4.31%)	
occurrences causally related to treatment / all	0 / 8	0 / 13	
deaths causally related to treatment / all	0 / 5	0 / 5	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			

subjects affected / exposed	3 / 246 (1.22%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunosuppressant drug level increased			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Computerised tomogram thorax abnormal			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			

subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	3 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Blood stem cell transplant failure			
subjects affected / exposed	3 / 246 (1.22%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	1 / 3	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 2	
Drug dose omission			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Spinal fracture			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant failure			
subjects affected / exposed	0 / 246 (0.00%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Transfusion microchimerism			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	4 / 246 (1.63%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericardial effusion			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericarditis			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Acute polyneuropathy			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amnesia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lesion			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	3 / 246 (1.22%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Headache			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological decompensation			

subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Paraplegia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamus haemorrhage			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 246 (0.00%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anaemia			
subjects affected / exposed	3 / 246 (1.22%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			

subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aplasia pure red cell			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone marrow failure			
subjects affected / exposed	3 / 246 (1.22%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	11 / 246 (4.47%)	11 / 255 (4.31%)	
occurrences causally related to treatment / all	0 / 14	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	3 / 246 (1.22%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	1 / 3	1 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neutropenia			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	5 / 246 (2.03%)	5 / 255 (1.96%)	
occurrences causally related to treatment / all	0 / 6	1 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
Thrombocytopenia			
subjects affected / exposed	3 / 246 (1.22%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ear and labyrinth disorders			
Aural polyp			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Mydriasis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	10 / 246 (4.07%)	11 / 255 (4.31%)	
occurrences causally related to treatment / all	1 / 13	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophagitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal toxicity			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal haemorrhage			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			
subjects affected / exposed	10 / 246 (4.07%)	8 / 255 (3.14%)	
occurrences causally related to treatment / all	1 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Megacolon			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophagitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral pain			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
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	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	11 / 246 (4.47%)	7 / 255 (2.75%)	
occurrences causally related to treatment / all	0 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatic failure			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic vein occlusion			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venoocclusive liver disease			
subjects affected / exposed	5 / 246 (2.03%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain of skin			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
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	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stasis dermatitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic epidermal necrolysis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Urticaria			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	3 / 246 (1.22%)	5 / 255 (1.96%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 2	
Renal failure acute			
subjects affected / exposed	28 / 246 (11.38%)	41 / 255 (16.08%)	
occurrences causally related to treatment / all	0 / 38	0 / 46	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			

subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure chronic			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
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			
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myopathy			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess intestinal			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acinetobacter bacteraemia			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal cellulitis			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atypical mycobacterial infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	4 / 246 (1.63%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 4	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
BK virus infection			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain abscess			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bacterial sepsis			
subjects affected / exposed	3 / 246 (1.22%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchitis			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	4 / 246 (1.63%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Catheter site infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	3 / 246 (1.22%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral aspergillosis			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Citrobacter sepsis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 246 (0.81%)	5 / 255 (1.96%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	3 / 246 (1.22%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Corona virus infection			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus gastritis			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
subjects affected / exposed	3 / 246 (1.22%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cystitis bacterial			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus gastroenteritis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	10 / 246 (4.07%)	6 / 255 (2.35%)	
occurrences causally related to treatment / all	0 / 10	1 / 6	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cytomegalovirus viraemia			
subjects affected / exposed	11 / 246 (4.47%)	9 / 255 (3.53%)	
occurrences causally related to treatment / all	2 / 13	1 / 11	
deaths causally related to treatment / all	0 / 2	0 / 2	
Device related infection			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	0 / 246 (0.00%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis cytomegalovirus			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Encephalitis herpes			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Enterococcal bacteraemia			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis bacterial			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr viraemia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			

subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Escherichia sepsis			
subjects affected / exposed	3 / 246 (1.22%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital herpes			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic candidiasis			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Herpes simplex			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	4 / 246 (1.63%)	5 / 255 (1.96%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster ophthalmic			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human polyomavirus infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human herpesvirus 6 infection			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	3 / 246 (1.22%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	4 / 246 (1.63%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Meningitis aseptic			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			

subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia adenoviral			

subjects affected / exposed	1 / 246 (0.41%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	19 / 246 (7.72%)	15 / 255 (5.88%)	
occurrences causally related to treatment / all	0 / 20	1 / 18	
deaths causally related to treatment / all	0 / 5	0 / 6	
Pneumonia fungal			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia escherichia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia herpes viral			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia cytomegaloviral			
subjects affected / exposed	3 / 246 (1.22%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia legionella			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			

subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia viral			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mycosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	14 / 246 (5.69%)	20 / 255 (7.84%)	
occurrences causally related to treatment / all	0 / 14	1 / 23	
deaths causally related to treatment / all	0 / 3	0 / 8	
Respiratory tract infection			
subjects affected / exposed	4 / 246 (1.63%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	10 / 246 (4.07%)	9 / 255 (3.53%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 7	0 / 3	
Sialoadenitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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 / 246 (0.41%)	3 / 255 (1.18%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis fungal			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin infection			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			

subjects affected / exposed	5 / 246 (2.03%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic mycosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-ovarian abscess			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 246 (1.63%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	3 / 246 (1.22%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection fungal			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral haemorrhagic cystitis			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Decreased appetite			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	4 / 246 (1.63%)	4 / 255 (1.57%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 246 (0.00%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	1 / 246 (0.41%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fluid overload			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 246 (0.81%)	2 / 255 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	2 / 246 (0.81%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	2 / 246 (0.81%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	1 / 246 (0.41%)	0 / 255 (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	ASP0113 5mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	244 / 246 (99.19%)	254 / 255 (99.61%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	66 / 246 (26.83%)	83 / 255 (32.55%)	
occurrences (all)	78	96	
Hypotension			
subjects affected / exposed	39 / 246 (15.85%)	36 / 255 (14.12%)	
occurrences (all)	50	37	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	30 / 246 (12.20%)	34 / 255 (13.33%)	
occurrences (all)	39	43	
Injection site erythema			
subjects affected / exposed	49 / 246 (19.92%)	5 / 255 (1.96%)	
occurrences (all)	72	5	
Fatigue			
subjects affected / exposed	58 / 246 (23.58%)	69 / 255 (27.06%)	
occurrences (all)	65	80	
Chills			
subjects affected / exposed	36 / 246 (14.63%)	44 / 255 (17.25%)	
occurrences (all)	46	59	
Catheter site pain			
subjects affected / exposed	22 / 246 (8.94%)	21 / 255 (8.24%)	
occurrences (all)	29	23	
Injection site induration			
subjects affected / exposed	38 / 246 (15.45%)	3 / 255 (1.18%)	
occurrences (all)	57	3	
Mucosal inflammation			
subjects affected / exposed	75 / 246 (30.49%)	101 / 255 (39.61%)	
occurrences (all)	94	147	
Malaise			
subjects affected / exposed	15 / 246 (6.10%)	10 / 255 (3.92%)	
occurrences (all)	15	11	
Injection site swelling			
subjects affected / exposed	24 / 246 (9.76%)	4 / 255 (1.57%)	
occurrences (all)	36	4	
Injection site pain			
subjects affected / exposed	193 / 246 (78.46%)	47 / 255 (18.43%)	
occurrences (all)	1053	83	
Oedema			
subjects affected / exposed	35 / 246 (14.23%)	21 / 255 (8.24%)	
occurrences (all)	39	24	
Oedema peripheral			
subjects affected / exposed	66 / 246 (26.83%)	69 / 255 (27.06%)	
occurrences (all)	88	95	

Pain			
subjects affected / exposed	27 / 246 (10.98%)	32 / 255 (12.55%)	
occurrences (all)	34	34	
Pyrexia			
subjects affected / exposed	123 / 246 (50.00%)	128 / 255 (50.20%)	
occurrences (all)	180	195	
Immune system disorders			
Chronic graft versus host disease			
subjects affected / exposed	62 / 246 (25.20%)	60 / 255 (23.53%)	
occurrences (all)	110	109	
Engraftment syndrome			
subjects affected / exposed	13 / 246 (5.28%)	9 / 255 (3.53%)	
occurrences (all)	15	9	
Chronic graft versus host disease in skin			
subjects affected / exposed	37 / 246 (15.04%)	46 / 255 (18.04%)	
occurrences (all)	40	51	
Chronic graft versus host disease in liver			
subjects affected / exposed	30 / 246 (12.20%)	35 / 255 (13.73%)	
occurrences (all)	43	45	
Chronic graft versus host disease in intestine			
subjects affected / exposed	20 / 246 (8.13%)	21 / 255 (8.24%)	
occurrences (all)	22	28	
Hypogammaglobulinaemia			
subjects affected / exposed	20 / 246 (8.13%)	19 / 255 (7.45%)	
occurrences (all)	20	20	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	40 / 246 (16.26%)	44 / 255 (17.25%)	
occurrences (all)	50	53	
Cough			
subjects affected / exposed	55 / 246 (22.36%)	60 / 255 (23.53%)	
occurrences (all)	71	71	
Epistaxis			

subjects affected / exposed	34 / 246 (13.82%)	23 / 255 (9.02%)	
occurrences (all)	37	28	
Hiccups			
subjects affected / exposed	22 / 246 (8.94%)	20 / 255 (7.84%)	
occurrences (all)	24	21	
Hypoxia			
subjects affected / exposed	17 / 246 (6.91%)	10 / 255 (3.92%)	
occurrences (all)	21	12	
Nasal congestion			
subjects affected / exposed	8 / 246 (3.25%)	18 / 255 (7.06%)	
occurrences (all)	8	20	
Oropharyngeal pain			
subjects affected / exposed	30 / 246 (12.20%)	41 / 255 (16.08%)	
occurrences (all)	33	42	
Rhinorrhoea			
subjects affected / exposed	18 / 246 (7.32%)	16 / 255 (6.27%)	
occurrences (all)	19	17	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	40 / 246 (16.26%)	44 / 255 (17.25%)	
occurrences (all)	42	53	
Depression			
subjects affected / exposed	11 / 246 (4.47%)	18 / 255 (7.06%)	
occurrences (all)	11	18	
Insomnia			
subjects affected / exposed	72 / 246 (29.27%)	76 / 255 (29.80%)	
occurrences (all)	86	85	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	33 / 246 (13.41%)	31 / 255 (12.16%)	
occurrences (all)	66	47	
Aspartate aminotransferase increased			
subjects affected / exposed	30 / 246 (12.20%)	30 / 255 (11.76%)	
occurrences (all)	49	45	
Blood alkaline phosphatase increased			

subjects affected / exposed	18 / 246 (7.32%)	17 / 255 (6.67%)	
occurrences (all)	23	24	
Blood bilirubin increased			
subjects affected / exposed	21 / 246 (8.54%)	23 / 255 (9.02%)	
occurrences (all)	43	48	
Blood creatinine increased			
subjects affected / exposed	22 / 246 (8.94%)	29 / 255 (11.37%)	
occurrences (all)	27	42	
Platelet count decreased			
subjects affected / exposed	28 / 246 (11.38%)	37 / 255 (14.51%)	
occurrences (all)	49	83	
Neutrophil count decreased			
subjects affected / exposed	28 / 246 (11.38%)	33 / 255 (12.94%)	
occurrences (all)	62	70	
Gamma-glutamyltransferase increased			
subjects affected / exposed	15 / 246 (6.10%)	13 / 255 (5.10%)	
occurrences (all)	26	24	
Transaminases increased			
subjects affected / exposed	18 / 246 (7.32%)	10 / 255 (3.92%)	
occurrences (all)	19	11	
Weight decreased			
subjects affected / exposed	12 / 246 (4.88%)	15 / 255 (5.88%)	
occurrences (all)	15	15	
White blood cell count decreased			
subjects affected / exposed	24 / 246 (9.76%)	23 / 255 (9.02%)	
occurrences (all)	45	65	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	15 / 246 (6.10%)	10 / 255 (3.92%)	
occurrences (all)	17	12	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	22 / 246 (8.94%)	22 / 255 (8.63%)	
occurrences (all)	28	24	
Nervous system disorders			

Dizziness			
subjects affected / exposed	33 / 246 (13.41%)	33 / 255 (12.94%)	
occurrences (all)	44	38	
Neuropathy peripheral			
subjects affected / exposed	14 / 246 (5.69%)	17 / 255 (6.67%)	
occurrences (all)	17	17	
Headache			
subjects affected / exposed	103 / 246 (41.87%)	103 / 255 (40.39%)	
occurrences (all)	150	153	
Dysgeusia			
subjects affected / exposed	23 / 246 (9.35%)	22 / 255 (8.63%)	
occurrences (all)	24	22	
Tremor			
subjects affected / exposed	23 / 246 (9.35%)	46 / 255 (18.04%)	
occurrences (all)	24	49	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	66 / 246 (26.83%)	75 / 255 (29.41%)	
occurrences (all)	146	160	
Febrile neutropenia			
subjects affected / exposed	91 / 246 (36.99%)	92 / 255 (36.08%)	
occurrences (all)	101	98	
Neutropenia			
subjects affected / exposed	65 / 246 (26.42%)	65 / 255 (25.49%)	
occurrences (all)	99	98	
Leukopenia			
subjects affected / exposed	20 / 246 (8.13%)	23 / 255 (9.02%)	
occurrences (all)	51	56	
Pancytopenia			
subjects affected / exposed	21 / 246 (8.54%)	18 / 255 (7.06%)	
occurrences (all)	21	19	
Thrombocytopenia			
subjects affected / exposed	49 / 246 (19.92%)	48 / 255 (18.82%)	
occurrences (all)	131	111	
Eye disorders			

Conjunctivitis			
subjects affected / exposed	12 / 246 (4.88%)	17 / 255 (6.67%)	
occurrences (all)	12	18	
Dry eye			
subjects affected / exposed	42 / 246 (17.07%)	37 / 255 (14.51%)	
occurrences (all)	45	39	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	13 / 246 (5.28%)	8 / 255 (3.14%)	
occurrences (all)	15	11	
Abdominal pain			
subjects affected / exposed	62 / 246 (25.20%)	60 / 255 (23.53%)	
occurrences (all)	84	83	
Abdominal distension			
subjects affected / exposed	15 / 246 (6.10%)	22 / 255 (8.63%)	
occurrences (all)	18	22	
Abdominal pain upper			
subjects affected / exposed	26 / 246 (10.57%)	33 / 255 (12.94%)	
occurrences (all)	32	37	
Diarrhoea			
subjects affected / exposed	166 / 246 (67.48%)	167 / 255 (65.49%)	
occurrences (all)	242	244	
Constipation			
subjects affected / exposed	90 / 246 (36.59%)	103 / 255 (40.39%)	
occurrences (all)	119	128	
Dry mouth			
subjects affected / exposed	30 / 246 (12.20%)	25 / 255 (9.80%)	
occurrences (all)	35	31	
Dyspepsia			
subjects affected / exposed	31 / 246 (12.60%)	25 / 255 (9.80%)	
occurrences (all)	35	27	
Gastrooesophageal reflux disease			
subjects affected / exposed	24 / 246 (9.76%)	16 / 255 (6.27%)	
occurrences (all)	25	17	
Gastritis			

subjects affected / exposed	19 / 246 (7.72%)	19 / 255 (7.45%)	
occurrences (all)	20	19	
Haemorrhoids			
subjects affected / exposed	27 / 246 (10.98%)	23 / 255 (9.02%)	
occurrences (all)	28	26	
Nausea			
subjects affected / exposed	178 / 246 (72.36%)	177 / 255 (69.41%)	
occurrences (all)	273	261	
Oral pain			
subjects affected / exposed	19 / 246 (7.72%)	16 / 255 (6.27%)	
occurrences (all)	20	17	
Proctalgia			
subjects affected / exposed	20 / 246 (8.13%)	20 / 255 (7.84%)	
occurrences (all)	23	20	
Stomatitis			
subjects affected / exposed	79 / 246 (32.11%)	69 / 255 (27.06%)	
occurrences (all)	105	96	
Vomiting			
subjects affected / exposed	125 / 246 (50.81%)	122 / 255 (47.84%)	
occurrences (all)	195	178	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	13 / 246 (5.28%)	16 / 255 (6.27%)	
occurrences (all)	17	23	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	29 / 246 (11.79%)	30 / 255 (11.76%)	
occurrences (all)	31	32	
Dry skin			
subjects affected / exposed	25 / 246 (10.16%)	20 / 255 (7.84%)	
occurrences (all)	26	20	
Rash maculo-papular			
subjects affected / exposed	12 / 246 (4.88%)	13 / 255 (5.10%)	
occurrences (all)	15	17	
Erythema			

subjects affected / exposed	34 / 246 (13.82%)	28 / 255 (10.98%)	
occurrences (all)	50	37	
Pruritus			
subjects affected / exposed	59 / 246 (23.98%)	67 / 255 (26.27%)	
occurrences (all)	67	85	
Rash			
subjects affected / exposed	51 / 246 (20.73%)	52 / 255 (20.39%)	
occurrences (all)	67	61	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	20 / 246 (8.13%)	29 / 255 (11.37%)	
occurrences (all)	25	33	
Haematuria			
subjects affected / exposed	7 / 246 (2.85%)	15 / 255 (5.88%)	
occurrences (all)	8	15	
Pollakiuria			
subjects affected / exposed	8 / 246 (3.25%)	14 / 255 (5.49%)	
occurrences (all)	9	16	
Renal failure			
subjects affected / exposed	17 / 246 (6.91%)	16 / 255 (6.27%)	
occurrences (all)	19	17	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	30 / 246 (12.20%)	27 / 255 (10.59%)	
occurrences (all)	42	30	
Muscle spasms			
subjects affected / exposed	14 / 246 (5.69%)	19 / 255 (7.45%)	
occurrences (all)	15	25	
Bone pain			
subjects affected / exposed	10 / 246 (4.07%)	13 / 255 (5.10%)	
occurrences (all)	12	14	
Back pain			
subjects affected / exposed	44 / 246 (17.89%)	39 / 255 (15.29%)	
occurrences (all)	52	39	
Muscular weakness			

subjects affected / exposed	10 / 246 (4.07%)	14 / 255 (5.49%)	
occurrences (all)	10	15	
Neck pain			
subjects affected / exposed	16 / 246 (6.50%)	10 / 255 (3.92%)	
occurrences (all)	18	10	
Myalgia			
subjects affected / exposed	19 / 246 (7.72%)	19 / 255 (7.45%)	
occurrences (all)	23	22	
Musculoskeletal pain			
subjects affected / exposed	19 / 246 (7.72%)	14 / 255 (5.49%)	
occurrences (all)	21	14	
Pain in extremity			
subjects affected / exposed	32 / 246 (13.01%)	30 / 255 (11.76%)	
occurrences (all)	37	31	
Infections and infestations			
Clostridium difficile infection			
subjects affected / exposed	17 / 246 (6.91%)	16 / 255 (6.27%)	
occurrences (all)	18	16	
BK virus infection			
subjects affected / exposed	13 / 246 (5.28%)	13 / 255 (5.10%)	
occurrences (all)	15	13	
Cytomegalovirus infection			
subjects affected / exposed	45 / 246 (18.29%)	51 / 255 (20.00%)	
occurrences (all)	68	64	
Cytomegalovirus viraemia			
subjects affected / exposed	87 / 246 (35.37%)	96 / 255 (37.65%)	
occurrences (all)	132	141	
Device related infection			
subjects affected / exposed	16 / 246 (6.50%)	16 / 255 (6.27%)	
occurrences (all)	18	16	
Escherichia urinary tract infection			
subjects affected / exposed	13 / 246 (5.28%)	11 / 255 (4.31%)	
occurrences (all)	20	11	
Epstein-Barr virus infection			
subjects affected / exposed	15 / 246 (6.10%)	13 / 255 (5.10%)	
occurrences (all)	16	15	

Folliculitis			
subjects affected / exposed	8 / 246 (3.25%)	14 / 255 (5.49%)	
occurrences (all)	8	18	
Oral candidiasis			
subjects affected / exposed	17 / 246 (6.91%)	27 / 255 (10.59%)	
occurrences (all)	18	31	
Nasopharyngitis			
subjects affected / exposed	15 / 246 (6.10%)	12 / 255 (4.71%)	
occurrences (all)	15	14	
Oral herpes			
subjects affected / exposed	8 / 246 (3.25%)	17 / 255 (6.67%)	
occurrences (all)	13	18	
Pneumonia			
subjects affected / exposed	13 / 246 (5.28%)	13 / 255 (5.10%)	
occurrences (all)	13	13	
Upper respiratory tract infection			
subjects affected / exposed	22 / 246 (8.94%)	27 / 255 (10.59%)	
occurrences (all)	24	36	
Staphylococcal bacteraemia			
subjects affected / exposed	20 / 246 (8.13%)	17 / 255 (6.67%)	
occurrences (all)	23	20	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	72 / 246 (29.27%)	91 / 255 (35.69%)	
occurrences (all)	89	109	
Dehydration			
subjects affected / exposed	13 / 246 (5.28%)	13 / 255 (5.10%)	
occurrences (all)	31	16	
Diabetes mellitus			
subjects affected / exposed	17 / 246 (6.91%)	8 / 255 (3.14%)	
occurrences (all)	19	8	
Fluid overload			
subjects affected / exposed	11 / 246 (4.47%)	14 / 255 (5.49%)	
occurrences (all)	16	14	
Hyperglycaemia			

subjects affected / exposed	54 / 246 (21.95%)	66 / 255 (25.88%)	
occurrences (all)	81	90	
Hyperkalaemia			
subjects affected / exposed	30 / 246 (12.20%)	23 / 255 (9.02%)	
occurrences (all)	43	40	
Hypocalcaemia			
subjects affected / exposed	28 / 246 (11.38%)	37 / 255 (14.51%)	
occurrences (all)	51	58	
Hypoalbuminaemia			
subjects affected / exposed	24 / 246 (9.76%)	30 / 255 (11.76%)	
occurrences (all)	53	43	
Hyperuricaemia			
subjects affected / exposed	15 / 246 (6.10%)	10 / 255 (3.92%)	
occurrences (all)	17	14	
Hypokalaemia			
subjects affected / exposed	92 / 246 (37.40%)	83 / 255 (32.55%)	
occurrences (all)	140	120	
Hypomagnesaemia			
subjects affected / exposed	113 / 246 (45.93%)	113 / 255 (44.31%)	
occurrences (all)	168	157	
Hyponatraemia			
subjects affected / exposed	26 / 246 (10.57%)	25 / 255 (9.80%)	
occurrences (all)	32	42	
Hypophosphataemia			
subjects affected / exposed	24 / 246 (9.76%)	27 / 255 (10.59%)	
occurrences (all)	28	30	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2013	The changes include: Removal of all language referencing the donor sub-study. Added to Inclusion Criteria No. 10: clarification that male subjects and their female spouse/partners who are of child bearding potential must be using diaphragms or condoms starting at Screening and continue thought the treatment period and for 90 days after the final study drug administration. Added details to Exclusion Criteria No. 10: the components of the vaccine aminoglycoside antibiotics (kanamycin and the like used for the vaccine production). Added to Exclusion Criteria No. 13: Other subjects considered ineligible by the investigator/sub-investigator. Removal of all language referencing the Home Health Care (HHC) provider and procedures. Added a detailed table to show the time ranges of the specific examinations, observations, etc. Removal of specific language referencing portions of the PGx sub-study procedures that will not be followed in Japan. Removal of references that study drug should be returned to the sponsor or depot. Removed references to drug may be destroyed at the study center. Added that the head of the study drug store manager should take responsibility for the accountability, storage, inventory, reconciliation and returns. Removed the option to have others designated by the Sponsor perform subject unblinding. Revised SAE reporting contact information. Revised who is responsible for submitting expedited reports to the Japanese authorities. Revised that the investigator will report SAEs to the head of the study center and ensure reporting to JUTOKUNA YUUGAIJISHOU. Responsibilities of the investigator were added to judge when the follow up of an SAE is no longer necessary. Responsibilities of the study center head were added with regards to obtaining and reporting new information on serious and unexpected adverse reactions. Added in the always report as serious list to the study appendices.
01 October 2013	The changes include: Added additional actions for the investigator to take when they do not follow the protocol for medically inevitable reasons in order to avoid urgent risks for subjects. Deleted the rest of world confidentiality language and added Japan confidentiality language. Deleted the rest of world publication language and added Japan publication language. Deleted the rest of world insurance language and procedures and added Japan insurance language.

28 March 2014	The changes include: Added Multi Gated Acquisition Scan (MUGA) as an acceptable procedure to determine HCT-CI criteria. Revised language to indicate that the first dose of study drug can now be administered within 72 hours prior to the start of conditioning therapy.Added language to state that the platelet count must be greater than or equal to 50,000 mm3 within 3 days prior to all study drug injections, and added clarification that results must be converted to SI units. Added language for donating peripheral stem cells prior to the initiation of mobilization therapy (eg G-CSF) for the purpose of donor blood sample collection.Added criteria and methods language regarding the planned futility analyses.Added language to Inclusion Criteria 4 to state acceptable allelles crossmatch typing.Added language to Inclusion Criteria 6 (g)(i) to specify how refractory anemia is defined. Removed Wingard reference. Added language allowing serum pregnancy testing at Screening and subsequent testing days. Specified that the birth control requirement is for heterosexually active participants. Movedlanguage regarding acceptable forms of birth control to another inclusion criterion and increased the duration of birth control use while in the study. Added language regarding acceptable forms of birth control and male sterilization and increased duration of birth control use while in the study.Revised language to increase duration of birth control use while in the study. Revised the HCT-CI score to exclude subjects that have a comorbidity score of ≥ 4. Specified Polymerase Chain Reaction (PCR) as the type of hepatitis C RNA. Added a statement to clarify components used in manufacturing of the vaccine, kanamycin. Added that cord transplants and haploidentical transplant subjects are excluded because they are expected to have reduced response to ASP0113. Added that subjects with a platelet count of less than 50,000 mm3 within 3 days prior to randomization are excl
28 March 2014	The changes include: Added that subjects with aplastic anemia or multiple myeloma are excluded. In the Treatment and Study Discontinuation Section, added the criteria that subjects that fail to receive one or more doses of study drug after the first injection but are able to continue in the trial, should not be terminated. Also, included the criteria to allow the PI to use their medical discretion in determining whether a subject should continue with study drug treatment and/or the study. In the Treatment Only Discontinuation Section, added criteria regarding anaphylaxis, seizure, and participation in other interventional trials. Also revised language to clarify follow-up visit requirements for safety reporting purposes. Added instructions of the process for subjects that receive at least one dose of study drug, but do not complete the vaccination regimen. Added language stating that intravenous dose of Aciclovir may be rounded up to the nearest 100 mg. Revised value for the protocol-defined CMV viral load to 1000 IU/mL. a) Revised and added language to allow the Screening visit and Visit 2 to occur on the same day, b) allow the use of local laboratory results to determine eligibility at the Screening Visit,and c) to outline the rescreen/repeat lab parameters during the Screening Period. Added language to state that Screening safety laboratory assessments are to be completed by the local laboratory and beginning at Visit 2, all laboratory assessment are to be completed by the central laboratory. Added row to Table 1 for Karnofsky Performance scale and text to clearly state this will be assessed at Visits 2, 5, 7, 9, 11, 13, and 14. Increased the window to ± 4 days for the CMV & GVHD assessments on Day 7/Week 1(A1). Added a window of ± 10 minutes for vital signs and reactogenicity evaluations done 60 minutes after injection. Revised language regarding length of time concomitant medication information will be captured after the last administration of study drug.

28 March 2014	The changes include: Removed the optional Abbott whole blood sub-study. Added additional data points to be collected regarding transplant information, such as volume infused, donor race and ethnicity. Added language regarding SAE reporting requirements during the long-term follow-up period. Added language regarding non-clinical data. Clarify by what method the vaccine schedule was determined. Removed first bullet regarding an exploratory analysis and revised language in appendix. Added language to indicate current regulatory status of the Abbott device being used for CMV viral load testing. Removed language related to how to record the grade of GVHD and added a bullet to indicate how to assess chronic GVHD. Added language to indicate how to capture the day of engraftment. Revised language to indicate the information that will be collected by the site on the HEA. Total blood volume to be collected for the study is increased. Added language to include the Data Monitoring Committee's responsibilities and planned futility analysis. Revised language for the potential of additional components to be incorporated into the composite endpoint. Added reference and include table of protocol defined definitions of comorbidities for the HCT-Comorbidity Index. Revised definition of CMV Retinitis diagnosis to include in vitreous fluid by culture or PCR. Revised language to remove the last sub-bullet in the list regarding all cause mortalities excluding the expected adverse drug reactions (ADRs) with a fatal outcome.
20 May 2014	The changes include: Section III – List of Abbreviations and Key Terms-Added MUGA Multi Gated Acquisition Scan Modified HCT-CI Score- Amended to "The subject's Modified HCT-CI score should must be determined during the Screening period using the history and laboratory results obtained on the day of Screening. Pulmonary function tests (PFTs), multi gated acquisition scans (MUGAs), and/or echocardiograms performed within 6 months (180 days) prior to Screening can be used for scoring pulmonary and cardiac comorbidities."Modified HCT-CI Comorbidity Definitions and Scores - Amended to"*Pulmonary function tests (PFTs), multi gated acquisition scans (MUGAs), and/or echocardiograms performed within 6 months (180 days) prior to Screening may be used for scoring pulmonary and cardiac comorbidities." When assessing Renal function, to convert creatinine from micromoles per liter (Umole/L) to milligrams per deciliter (mg/dL), divide micromoles per liter by 88.4 (Umole/L ÷ 88.4 = mg/dL). The definitions for each comorbidity based on definitions published by Sorror in 2013 are provided below: Protocol Defined Definitions of Comoribidities for the HCT-Comorbidity Index. Arrhythmia (score 1): Any type of arrhythmia that has necessitated the delivery of a specific anti-arrhythmia treatment at any time in the patient's past medical history. A score is assigned even if the patient was in normal sinus rhythm at the time of data acquisition or at the landmark date. No score is assigned to transient arrhythmias that never required treatment.
04 December 2015	The changes include: Parts 1 and 2 of the study design are merged into a single 1-part study. Composite endpoint of overall mortality and cytomegalovirus (CMV) end organ disease (EOD) through 1 year post-transplant will be assessed as a primary endpoint. Incidence of grade 3 treatment-emergent infections other than CMV and Time to Grade 3 treatment emergent infections other than CMV were reclassified from secondary to exploratory endpoints. Clarity provided regarding discontinuation subjects who are enrolled in the study and for whom study treatment is permanently discontinued prematurely for any reason. Specify that approximately 500 subjects will be enrolled and receive study drug in the study. Specify that with respect to incidence of other efficacy-related clinical outcomes, subjects with insufficient data to determine status will be assumed to have had the event in question.
04 August 2016	The changes include: All women < 50 years of age who are not documented to be surgically sterile must have a negative urine or serum pregnancy test at screening and prior to each dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In Oct 2014 data monitoring committee informed Astellas of the results of the first futility analysis. The FDA considered data for 68 participants included in futility analysis compromised and asked that it is not included in final efficacy analysis.

Notes: