Clinical trial results:
A randomised trial of the European and American Osteosarcoma Study group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy

Summary

EudraCT number	2004-000242-20
Trial protocol	FI NO BE IE AT CZ GB
Global end of trial date	31 December 2018

Results information

Result version number	v1 (current)
This version publication date	05 September 2020
First version publication date	05 September 2020

Trial information

Trial identification

Sponsor protocol code	EURAMOS 1

Additional study identifiers

ISRCTN number	ISRCTN67613327
ClinicalTrials.gov id (NCT number)	NCT00134030
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical Research Council
Sponsor organisation address	90 High Holborn, London, United Kingdom, WC1V 6LJ
Public contact	EURAMOS trial team, MRC CTU at UCL, mrcctu.euramos@ucl.ac.uk
Scientific contact	EURAMOS trial team, MRC CTU at UCL, mrcctu.euramos@ucl.ac.uk

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 November 2014
Global end of trial reached?	Yes
Global end of trial date	31 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal aim of this study is to find out whether giving extra treatment for osteosarcoma in addition to the standard 3-drug chemotherapy, methotrexate, doxorubicin and cisplatin (MAP), will improve the overall results for patients.
Initially, all patients will receive two cycles of pre-operative MAP. After the tumour has been removed by surgery, it will be assessed for histological response: good response is defined as less than 10% viable tumour, poor response is defined as 10% or more viable tumour.
The primary objectives of the trial are:
1. To investigate whether the addition of extra chemotherapy agents (ifosfamide and etoposide) to their post-operative chemotherapy improves event-free survival in patients who have a poor response to pre-operative chemotherapy
2. To investigate whether maintenance therapy (interferon alfa) following chemotherapy improves event-free survival in patients who have a good response to pre-operative chemotherapy.

Protection of trial subjects:

Patients provided informed consent prior to entering the trial. All patients were followed and treated by qualified clinicians and surgeons in specialised teams.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 August 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 34
Country: Number of subjects enrolled	United Kingdom: 166
Country: Number of subjects enrolled	Austria: 20
Country: Number of subjects enrolled	Belgium: 44
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Canada: 47
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Germany: 298
Country: Number of subjects enrolled	Hungary: 19

Country: Number of subjects enrolled	Netherlands: 65
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Sweden: 33
Country: Number of subjects enrolled	Switzerland: 25
Country: Number of subjects enrolled	United States: 543
Worldwide total number of subjects	1334
EEA total number of subjects	701

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)	322
Adolescents (12-17 years)	740
Adults (18-64 years)	272
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	2260[1]
Number of subjects completed	1334

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Late histology: 83
Reason: Number of subjects	Wrong pre-op chemotherapy: 56
Reason: Number of subjects	Disease progression: 130
Reason: Number of subjects	Not recovered from pre-op treatment: 22
Reason: Number of subjects	Incomplete surgery: 40
Reason: Number of subjects	Could not randomised in time: 14
Reason: Number of subjects	Patient <5 years (good response): 6
Reason: Number of subjects	Physician decision: 10
Reason: Number of subjects	Consent withdrawn by subject: 403
Reason: Number of subjects	Uncertain response: 2
Reason: Number of subjects	Histological response unknown: 160

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number enrolled is the number of patients randomised. In the pre-assignment period, patients were registered to assess response.

Period 1

Period 1 title	Main trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MAP-GR

Arm description:

Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with good response after surgery (<10% viable tumour)

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

12000 mg/m2, given in weeks 4, 5, 9, 10, 15, 16, 20, 21, 24, 25, 28, 29.

Weeks 4-10 are pre-randomisation.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m2, given in weeks 1, 6, 12, 17, 22, and 26.
Weeks 1 and 6 are pre-randomisation.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

120 mg/m2, given in weeks 1, 6, 12, 17.
Weeks 1 and 6 are pre-randomisation.

Arm title	MAPifn

Arm description:

Methotrexate, Doxorubicin, Cisplatin plus pegylated interferon. Experimental arm for patients with good response after surgery (<10% viable tumour).

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

Dosage and administration details:

75 mg/m2, given in weeks 1, 6, 12, 17, 22, 26.
Weeks 1 and 6 are pre-randomisation.

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

12000 mg/m2, given in weeks 4, 5, 9, 10, 15, 16, 20, 21, 24, 25, 28, 29.
Weeks 4-10 are pre-randomisation.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

120 mg/m2, given in weeks 1, 6, 12, 17.
Weeks 1 and 6 are pre-randomisation.

Investigational medicinal product name	Pegylated interferon
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Weekly from week 30 (or recovery from toxicity from MAP) until week 104. 0.5-1.0 microgram/kg s.c. once weekly.

Arm title	MAP-PR

Arm description:

Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with poor response after surgery (>10% viable tumour).

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

12000 mg/m2, given in weeks 4, 5, 9, 10, 15, 16, 20, 21, 24, 25, 28, 29.
Weeks 4-10 are pre-randomisation.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m2, given in weeks 1, 6, 12, 17, 22, 26.
Weeks 1 and 6 are pre-randomisation.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

120 mg/m2, given in weeks 1, 6, 12, 17.
Weeks 1 and 6 are pre-randomisation.

Arm title	MAPIE

Arm description:

Methotrexate, Doxorubicin, Cisplatin, plus ifosfamide and etoposide. Experimental arm for patients with poor response after surgery (>10% viable tumour).

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

Dosage and administration details:

12000 mg/m2, given in weeks 4, 5, 9, 10, 15, 19, 23, 27, 31, 35, 39, 40.
Weeks 4-10 are pre-randomisation.

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m2, given in weeks 1, 6, 12, 20, 28, 36.
Weeks 1 and 6 are pre-randomisation.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

120 mg/m2, given in weeks 1, 6, 12, 28.
Weeks 1 and 6 are pre-randomisation.

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

14 g/m2, given in weeks 16, 24, 32.
9 g/m2 given in weeks 20 and 36.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

500 mg/m2, given in weeks 16, 24, 32.

Number of subjects in period 1	MAP-GR	MAPifn	MAP-PR
Started	359	357	310
Completed	359	357	310

Number of subjects in period 1	MAPIE
Started	308
Completed	308

Baseline characteristics

Reporting groups	
Reporting group title	MAP-GR
Reporting group description:	
Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with good response after surgery (<10% viable tumour)	
Reporting group title	MAPifn
Reporting group description:	
Methotrexate, Doxorubicin, Cisplatin plus pegylated interferon. Experimental arm for patients with good response after surgery (<10% viable tumour).	
Reporting group title	MAP-PR
Reporting group description:	
Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with poor response after surgery (>10% viable tumour).	
Reporting group title	MAPIE
Reporting group description:	
Methotrexate, Doxorubicin, Cisplatin, plus ifosfamide and etoposide. Experimental arm for patients with poor response after surgery (>10% viable tumour).	

Reporting group values	MAP-GR	MAPifn	MAP-PR
Number of subjects	359	357	310
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	94	77	85
Adolescents (12-17 years)	206	218	142
Adults (18-64 years)	59	62	83
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	14	14	15
inter-quartile range (Q1-Q3)	11 to 16	12 to 16	11 to 18
Gender categorical Units: Subjects			
Female	148	147	136
Male	211	210	174
Site of tumour Units: Subjects			
Femur	179	191	154
Tibia	113	102	75
Fibula	14	20	17
Humerus	36	33	39
Radius	5	5	4
Ulna	2	0	2

Scapula/clavicle	2	1	3
Pelvis/sacrum	5	5	8
Rib	3	0	3
Other	0	0	5
Location of tumour on the bone Units: Subjects			
Proximal	156	150	114
Diapysis	13	12	11
Distal	180	189	166
N/A (not long bone)	10	6	19
Pathological fracture at diagnosis Units: Subjects			
No	321	308	276
Yes	37	49	34
Data missing	1	0	0
Lung metastases Units: Subjects			
No/possible	324	321	272
Yes	35	36	38
Histological classification Units: Subjects			
Conventional	320	322	288
Telangiectatic	25	20	11
Small cell	2	1	3
High-grade surface	3	5	5
Other	4	2	0
Data missing	5	7	3

Reporting group values	MAPIE	Total	
Number of subjects	308	1334	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	66	322	
Adolescents (12-17 years)	174	740	
Adults (18-64 years)	68	272	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	15		
inter-quartile range (Q1-Q3)	12 to 17	-	
Gender categorical Units: Subjects			
Female	117	548	
Male	191	786	

Site of tumour Units: Subjects			
Femur	166	690	
Tibia	76	366	
Fibula	13	64	
Humerus	27	135	
Radius	6	20	
Ulna	1	5	
Scapula/clavicle	2	8	
Pelvis/sacrum	11	29	
Rib	3	9	
Other	3	8	
Location of tumour on the bone Units: Subjects			
Proximal	109	529	
Diapysis	12	48	
Distal	168	703	
N/A (not long bone)	19	54	
Pathological fracture at diagnosis Units: Subjects			
No	270	1175	
Yes	35	155	
Data missing	3	4	
Lung metastases Units: Subjects			
No/possible	280	1197	
Yes	28	137	
Histological classification Units: Subjects			
Conventional	289	1219	
Telangiectatic	6	62	
Small cell	2	8	
High-grade surface	6	19	
Other	1	7	
Data missing	4	19	

End points

End points reporting groups

Reporting group title	MAP-GR
Reporting group description:	
Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with good response after surgery (<10% viable tumour)	
Reporting group title	MAPifn
Reporting group description:	
Methotrexate, Doxorubicin, Cisplatin plus pegylated interferon. Experimental arm for patients with good response after surgery (<10% viable tumour).	
Reporting group title	MAP-PR
Reporting group description:	
Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with poor response after surgery (>10% viable tumour).	
Reporting group title	MAPIE
Reporting group description:	
Methotrexate, Doxorubicin, Cisplatin, plus ifosfamide and etoposide. Experimental arm for patients with poor response after surgery (>10% viable tumour).	

Primary: Event-free survival at 3 years (primary analysis)

End point title	Event-free survival at 3 years (primary analysis)
End point description:	
Event-free survival is the time from randomisation until the first occurrence of local recurrence, new metastatic disease, progression of primary metastatic disease, secondary malignancy, or death. Patients without an even were censored at the date of last contact. These results are from the primary analyses, published in 2016 (poor response groups) and 2015 (good response group).	
End point type	Primary
End point timeframe:	
Event rate at 3 years	

End point values	MAP-GR	MAPifn	MAP-PR	MAPIE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	359	357	310	308
Units: Percentage				
number (confidence interval 95%)	74 (69 to 79)	77 (72 to 81)	55 (49 to 60)	53 (47 to 59)

Statistical analyses

Statistical analysis title	Good response group EFS
Statistical analysis description:	
Hazard ratio comparing event-free survival for patients with a good response after surgery.	
Comparison groups	MAP-GR v MAPifn

Number of subjects included in analysis	716
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.214
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.12

Statistical analysis title	Poor response group EFS

Statistical analysis description:

Hazard ratio comparing event-free survival for patients with a poor response after surgery.

Comparison groups	MAP-PR v MAPIE
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.23

Secondary: RMST (primary analysis)

End point title	RMST (primary analysis)[1]

End point description:

For the poor response group, there was evidence of non-proportional hazards, so secondary analysis was performed using restricted mean survival.

End point type	Secondary

End point timeframe:

RMST over 6 years from randomisation.

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis is only in the cohort of poor responders.

End point values	MAP-PR	MAPIE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	308		
Units: Months				
number (confidence interval 95%)	43.3 (40.1 to 46.4)	44.1 (41.1 to 47.1)		

Statistical analyses

Statistical analysis title	Poor response group EFS (RMST)
Statistical analysis description:	
Difference in RMST for poor response group (MAPIE - MAP-PR).	
Comparison groups	MAPIE v MAP-PR
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	4.9

Secondary: Event-free survival at 5 years (long-term analysis)

End point title	Event-free survival at 5 years (long-term analysis)

End point description:

Event-free survival is the time from randomisation until the first occurrence of local recurrence, new metastatic disease, progression of primary metastatic disease, secondary malignancy, or death. Patients without an even were censored at the date of last contact.

These results are from the long-term analysis, first presented at CTOS in November 2019.

End point type	Secondary

End point timeframe:

Event-free survival rate at 5 years

End point values	MAP-GR	MAPifn	MAP-PR	MAPIE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	359	357	310	308
Units: percent				
number (confidence interval 95%)	69 (65 to 74)	74 (70 to 80)	50 (45 to 55)	46 (41 to 52)

Statistical analyses

Statistical analysis title	Good response group EFS
Comparison groups	MAPifn v MAP-GR
Number of subjects included in analysis	716
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.212
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.1

Statistical analysis title	Poor response group EFS
Comparison groups	MAP-PR v MAPIE
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.993
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.24

Secondary: Overall survival at 5 years (long-term analysis)

End point title	Overall survival at 5 years (long-term analysis)

End point description:

Overall survival defined as time from randomisation until death from any cause, with patients censored at date of last follow-up.

Results of long-term analysis, first presented at CTOS conference in November 2019.

End point type	Secondary

End point timeframe:
Overall survival at 5 years

End point values	MAP-GR	MAPifn	MAP-PR	MAPIE
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	359	357	310	308
Units: percent				
number (confidence interval 95%)	84 (80 to 88)	84 (81 to 88)	68 (63 to 73)	68 (63 to 73)

Statistical analyses

Statistical analysis title	Good response group OS
Comparison groups	MAP-GR v MAPifn
Number of subjects included in analysis	716
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.804
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.33

Statistical analysis title	Poor response group OS
Comparison groups	MAP-PR v MAPIE
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.674
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.39

Secondary: RMST (long-term EFS analysis)

End point title	RMST (long-term EFS analysis)[2]

End point description:

For the poor response group, there was evidence of non-proportional hazards, so secondary analysis was performed using restricted mean survival.

End point type	Secondary

End point timeframe:

Randomisation to 11 years

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis is only in the cohort of poor responders.

End point values	MAP-PR	MAPIE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	308		
Units: months				
arithmetic mean (confidence interval 95%)	69.1 (62.9 to 75.2)	71.2 (64.9 to 77.4)		

Statistical analyses

Statistical analysis title	Poor response group EFS (RMST, long-term analysis)
Comparison groups	MAP-PR v MAPIE
Number of subjects included in analysis	618
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.667
Method	Difference in RMST
Parameter estimate	Mean difference (final values)
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	7.5

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From randomisation until 30 days after last protocol treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	MAP-GR
Reporting group description:	
Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with good response after surgery (<10% viable tumour)	
Reporting group title	MAPifn
Reporting group description:	
Methotrexate, Doxorubicin, Cisplatin plus pegylated interferon. Experimental arm for patients with good response after surgery (<10% viable tumour).	
Reporting group title	MAP-PR
Reporting group description:	
Methotrexate, Doxorubicin and Cisplatin. Control arm for patients with poor response after surgery (>10% viable tumour).	
Reporting group title	MAPIE
Reporting group description:	
Methotrexate, Doxorubicin, Cisplatin, plus ifosfamide and etoposide. Experimental arm for patients with poor response after surgery (>10% viable tumour).	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Toxicity was collected through SAEs, data on non serious adverse events are not available.

Serious adverse events	MAP-GR	MAPifn	MAP-PR
Total subjects affected by serious adverse events			
subjects affected / exposed	49 / 359 (13.65%)	76 / 357 (21.29%)	36 / 310 (11.61%)
number of deaths (all causes)	57	57	101
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ewing's sarcoma			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Myelodysplastic syndrome			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma stage I			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic venous thrombosis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery dissection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Chills			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication associated with device			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion site erythema			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion site thrombosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	3 / 359 (0.84%)	2 / 357 (0.56%)	6 / 310 (1.94%)
occurrences causally related to treatment / all	3 / 3	2 / 2	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	4 / 359 (1.11%)	3 / 357 (0.84%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	6 / 7	4 / 5	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity pneumonitis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 359 (0.00%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	1 / 359 (0.28%)	2 / 357 (0.56%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed mood			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device failure			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis in device			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 359 (0.28%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chemotherapeutic drug level increased			
subjects affected / exposed	2 / 359 (0.56%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug clearance decreased			
subjects affected / exposed	2 / 359 (0.56%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza B virus test positive			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

White blood cell count decreased			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprosthetic fracture			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound complication			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	2 / 359 (0.56%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Upper limb fracture			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Atrial thrombosis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 359 (0.00%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular insufficiency			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			

subjects affected / exposed	1 / 359 (0.28%)	2 / 357 (0.56%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular dysfunction			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Anosmia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral artery embolism			

subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytotoxic oedema			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dystonia			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	2 / 359 (0.56%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 359 (0.28%)	2 / 357 (0.56%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukoencephalopathy			

subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 359 (0.28%)	1 / 357 (0.28%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stupor			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	7 / 359 (1.95%)	5 / 357 (1.40%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	11 / 11	6 / 6	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	1 / 359 (0.28%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness bilateral			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Optic neuropathy			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 359 (0.28%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal ulcer			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Mouth ulceration			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 359 (0.28%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	3 / 359 (0.84%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	3 / 359 (0.84%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive liver disease			

subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy toxic			
subjects affected / exposed	1 / 359 (0.28%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Basedow's disease			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroiditis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone infarction			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint swelling			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic fracture			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 359 (0.00%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 359 (0.28%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 359 (0.00%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	2 / 359 (0.56%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			

subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	3 / 359 (0.84%)	6 / 357 (1.68%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	2 / 3	6 / 7	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ecthyma			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			

subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site cellulitis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site abscess			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			
subjects affected / exposed	0 / 359 (0.00%)	2 / 357 (0.56%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 359 (0.00%)	2 / 357 (0.56%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	2 / 310 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash pustular			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 359 (0.56%)	1 / 357 (0.28%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	2 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Septic arthritis staphylococcal			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal scalded skin syndrome			

subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal skin infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 359 (0.00%)	1 / 357 (0.28%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 359 (0.28%)	3 / 357 (0.84%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection staphylococcal			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 359 (0.28%)	0 / 357 (0.00%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MAPIE		

Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 308 (13.96%)		
number of deaths (all causes)	92		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	2 / 308 (0.65%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Ewing's sarcoma			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Papillary thyroid cancer			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal cell carcinoma stage I			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Jugular vein thrombosis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic venous thrombosis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral artery dissection				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chills				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Complication associated with device				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Impaired healing				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infusion site erythema				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infusion site thrombosis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Mucosal inflammation				
subjects affected / exposed	3 / 308 (0.97%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 308 (0.65%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemophagocytic lymphohistiocytosis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				

subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity pneumonitis			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleurisy			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Depressed mood			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mania			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			

subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device failure			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis in device			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood creatinine increased			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chemotherapeutic drug level increased			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Drug clearance decreased			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Influenza B virus test positive				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femoral neck fracture				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periprosthetic fracture				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Postoperative wound complication				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute left ventricular failure				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial thrombosis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				

subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiovascular insufficiency				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congestive cardiomyopathy				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	2 / 308 (0.65%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Left ventricular failure				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocarditis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				

subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular dysfunction				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular fibrillation				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Anosmia				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral artery embolism				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytotoxic oedema				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disturbance in attention				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dystonia				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				

subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiplegia				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukoencephalopathy				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Monoparesis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stupor				

subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Toxic encephalopathy			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	10 / 308 (3.25%)		
occurrences causally related to treatment / all	17 / 17		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness bilateral			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Optic neuropathy			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anal ulcer				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mouth ulceration				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				

subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stomatitis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Liver disorder			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Venoocclusive liver disease			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Acute kidney injury				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephropathy toxic				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Autoimmune thyroiditis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Basedow's disease				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inappropriate antidiuretic hormone secretion				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thyroiditis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Musculoskeletal and connective tissue disorders			
Bone infarction			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint swelling			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoporotic fracture			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pathological fracture			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Arthritis bacterial			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacterial sepsis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Catheter site infection			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Device related sepsis			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ecthyma			

subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
H1N1 influenza				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes simplex				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Implant site cellulitis				

subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Incision site abscess				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenic infection				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomonal sepsis				
subjects affected / exposed	0 / 308 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash pustular				

subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	4 / 308 (1.30%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Septic arthritis staphylococcal			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal scalded skin syndrome			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal skin infection			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varicella			

subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular device infection			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection staphylococcal			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 308 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MAP-GR	MAPifn	MAP-PR
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 359 (0.00%)	0 / 357 (0.00%)	0 / 310 (0.00%)

Non-serious adverse events	MAPIE		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 308 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2009	Recruitment period extended, with anticipated number of registered patients increase from 1400 to 2000. The target number of randomised patients stayed at 1260.
08 September 2011	Collection of quality of life data clarified, confirming that patients who don't complete an assessment at 5 weeks can still complete assessments at a later date. Clarification that Dexrazoxane cannot be used in the European Union.
13 May 2015	Duration of trial definition amended, to state that long term follow-up will continue for a minimum of 5 years after the final protocol treatment visit for the last patient. The trial will be closed after follow-up of patients is completed and all data queries have been resolved.

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 the good response patients (randomised to MAP-GR or MAPifn), 128 of 357 MAPifn patiients completed the planned protocol treatment.
Among poor response patients (randomised to MAP-PR or MAPie), 42% of registered patients were not randomised.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27569442

http://www.ncbi.nlm.nih.gov/pubmed/26033801

http://www.ncbi.nlm.nih.gov/pubmed/25421877