Clinical trial results:
A Phase III Randomized Trial of Gemtuzumab Ozogamicin (Mylotarg) Combined With Conventional Chemotherapy for De Novo Acute Myeloid Leukemia (AML) in Children, Adolescents, and Young Adults.

Summary

EudraCT number	2016-001533-28
Trial protocol	Outside EU/EEA
Global end of trial date	31 March 2013

Results information

Result version number	v1 (current)
This version publication date	25 July 2018
First version publication date	25 July 2018

Trial information

Trial identification

Sponsor protocol code	AAML0531

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00372593
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Children's Oncology Group
Sponsor organisation address	440 E. Huntington Drive, Arcadia, United States, CA 91006
Public contact	Clinical Trials.gov Call Center, Children’s Oncology Group, 1 6264470064, CTGOV@childrensoncologygroup.org
Scientific contact	Clinical Trials.gov Call Center, Children’s Oncology Group, 1 6264470064, CTGOV@childrensoncologygroup.org

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001733-PIP02-15
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	19 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the event free survival (EFS) and overall survival (OS) of de novo acute myeloid leukemia (AML) subjects randomized between the best current chemotherapy with or without gemtuzumab ozogamicin (GMTZ).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 958
Country: Number of subjects enrolled	Australia: 34
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Canada: 67
Worldwide total number of subjects	1069
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	4
Infants and toddlers (28 days-23 months)	205
Children (2-11 years)	435

Adolescents (12-17 years)	358
Adults (18-64 years)	67
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects with AML were enrolled and were randomly assigned to either standard five-course chemotherapy alone or to the same chemotherapy with two doses of gemtuzumab ozogamicin administered once in induction therapy 1 and once in intensification therapy 2. Subjects with down syndrome were non randomly assigned to receive standard chemotherapy.

Period 1

Period 1 title	overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: No Gemtuzumab ozogamicin

Arm description:

Cytarabine(ARA-C) intrathecally(IT) on Day 1 of induction therapy I,intravenous (IV) infusion (inf.) of 100 mg/m^2/twice daily ARA-C on Day 1-10; daunorubicin IV inf. of 50mg/m^2/dose on Day 1,3,5;IV inf. of 100 mg/m^2/dose etoposide on Day 1-5. After 3 weeks,ARA-C IT on Day 1 of induction therapy II,then IV ARA-C inf. of 100 mg/m^2/twice daily on Day 1-8;IV daunorubicin inf. of 50mg/m^2/dose on Day 1, 3, 5;etoposide IV infusion of 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks,ARA-C IT on Day 1 of intensification (INT) II;IV inf. of 1000 mg/m^2/twice daily of ARA-C on Day 1-4;mitoxantrone IV inf. of 12 mg/m^2/dose on Day 3-6. After 3 weeks,3 hour of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1, 2, 8, 9 of INT III and injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on basis of age.

Arm type	Active comparator
Investigational medicinal product name	Cytarabine
Investigational medicinal product code	ARA-C
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intrathecal use, Intravenous use

Dosage and administration details:

In IND therapy l, subjects received ARA-C (IT) at on Day 1 followed by an IV infusion of 100 mg/m^2/twice daily on Day 1-10. In Induction therapy ll, subjects received ARA-C (IT) on Day 1 followed by an IV infusion of 100 mg/m^2/twice daily on Day 1-8. In intensification therapy I, subjects received ARA-C (IT) on Day 1 followed by an IV infusion of 1000 mg/m^2/twice daily on Day 1-5. In intensification therapy ll, subjects received ARA-C (IT) followed by an IV infusion of 1000 mg/m^2/twice daily of ARA-C on Day 1-4. In intensification therapy III, subjects received an IV infusion of high dose of 3000 mg/m^2/per day of ARA-C on Day 1, 2, 8, and 9.

Investigational medicinal product name	Daunorubicin
Investigational medicinal product code	DAUN
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

In Induction therapy l, subjects received Daunorubicin IV over 6 hours 50mg/m^2/dose on Day 1,3 and 5. In Induction therapy ll, subjects received Daunorubicin IV over 6 hours 50mg/m^2/dose on Day 1,3 and 5.

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

Dosage and administration details:

In Induction therapy l, subjects received etoposide IV over 4 hours 100 mg/m^2/dose from Day 1 to Day 5. In Induction therapy ll, subjects received Etoposide IV over 4 hours 100 mg/m^2/dose from Day 1 to Day 5. In Intensification therapy I subjects received etoposide IV over 4 hours 150 mg/m^2/dose from Day 1 to Day 5.

Investigational medicinal product name	Mitoxantrone
Investigational medicinal product code	MITOX
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

In Intensification therapy II subjects received Mitoxantrone IV over 1 hour 12 mg/m^2/dose from Day 3 to 6.

Investigational medicinal product name	Asparaginase
Investigational medicinal product code	LASP
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

In Intensification therapy III subjects received an injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9.

Arm title	Arm B: Gemtuzumab ozogamicin

Arm description:

ARA-C (IT) on Day 1 of induction I (IND). IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-10;6 hr IV inf. daunorubicin (DAUN), 50mg/m^2/dose on Day 1,3,5; etoposide IV inf. of 100 mg/m^2/dose on Day 1-5;IV inf. of 3mg/m^2/dose of GMTZ on Day 6.After 3 weeks ARA-C IT, Day 1 of IND ll. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-8;IV inf. of 50 mg/m^2/dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m^2/dose on Day 1-5.After 3 weeks,ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m^2/twice daily of ARA-C,150 mg/m^2/dose of ETOP on Day 1-5. After 3 weeks; ARA-C IT on Day 1 of INT II; 1hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m^2/dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m^2/dose of GMTZ on Day 7. After 3 weeks of rest,3 hr of IV inf. of high dose of 3000 mg/m^2/twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m^2/dose of E. coli L-asparaginase on Day 2,9. Dose was administered on basis of age.

Arm type	Experimental
Investigational medicinal product name	Cytarabine
Investigational medicinal product code	AraC
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intrathecal use, Intravenous use

Dosage and administration details:

In IND therapy l, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m^2/twice daily on Day 1-10. In Induction therapy ll, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m^2/twice daily on Day 1-8. In intensification therapy I, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 1000 mg/m^2/twice daily on Day 1-5. In intensification therapy ll, subjects received ARA-C intrathecally followed by an IV infusion

of 1000 mg/m^2/twice daily of ARA-C on Day 1-4. In intensification therapy III, subjects received an IV infusion of high dose of 3000 mg/m^2/twice daily of ARA-C on Day 1, 2, 8, and 9.

Investigational medicinal product name	Daunorubicin
Investigational medicinal product code	DAUN
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

In Induction therapy I, subjects received Daunorubicin IV over 6 hours 50mg/m^2/dose on Day 1,3 and 5. In Induction therapy II, subjects received Daunorubicin IV over 6 hours 50 mg/m^2/dose on Day 1,3 and 5.

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

Dosage and administration details:

In Induction therapy l, subjects received Etoposide IV over 4 hours 100 mg/m^2/dose from Day 1 to Day 5. In Induction therapy ll, subjects received Etoposide IV over 4 hours 100 mg/m^2/dose from Day 1 to Day 5. In Intensification therapy I subjects received Etoposide IV over 4 hours 150 mg/m^2/dose from Day 1 to Day 5.

Investigational medicinal product name	Mitoxantrone
Investigational medicinal product code	MITOX
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

In Intensification therapy II subjects received Mitoxantrone IV over 1 hour 3mg/m^2/dose from Day 3 to 6.

Investigational medicinal product name	Asparaginase
Investigational medicinal product code	LASP
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

In Intensification therapy III, subjects received E.coli asparaginase an injection of 6000 IU/m^2/dose at Day 2 and Day 9.

Investigational medicinal product name	Gemtuzimab Ozogamicin
Investigational medicinal product code	GMTZ
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

In induction therapy I, subjects received Gemtuzumab Ozogamicin IV over 2 hours 3mg/m^2/dose at Day 6. In Intensification therapy II, subjects received Gemtuzumab Ozogamicin IV over 2 hours 3mg/m^2/dose at Day 7.

Arm title	Arm A: No Gemtuzumab ozogamicin (Down syndrome)

Arm description:

ARA-C (IT) on Day 1 of IND I. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m^2/dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy ll, then IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m^2/dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification II; a 1 hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4;1 hr IV inf. of mitoxantrone 12 mg/m^2/dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1,2,8,9 of intensification therapy III, an injection of E. Coli L-

asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on the basis of age of the subjects.

Arm type	Experimental
Investigational medicinal product name	Cytarabine
Investigational medicinal product code	ARA-C
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intrathecal use, Intravenous use

Dosage and administration details:

In Induction therapy l, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m^2/twice daily on Day 1-10. In Induction therapy ll, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m^2/twice on Day 1-8. In intensification therapy I, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 1000 mg/m^2/twice daily on Day 1-5. In intensification therapy ll, subjects received ARA-C intrathecally followed by an IV infusion of 1000 mg/m^2/twice daily of ARA-C on Day 1-4. In intensification therapy III, subjects received an IV infusion of high dose of 3000 mg/m^2/per day of ARA-C on Day 1, 2, 8 and 9.

Investigational medicinal product name	Mitoxantrone
Investigational medicinal product code	MITOX
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

In Intensification therapy II subjects received Mitoxantrone IV over 1 hour 12 mg/m^2/dose from Day 3 to 6.

Investigational medicinal product name	Asparaginase
Investigational medicinal product code	LASP
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

In Intensification therapy III, subjects received an injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9.

Investigational medicinal product name	Daunorubicin
Investigational medicinal product code	DAUN
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

In induction therapy I, subjects received Daunorubicin IV over 6 hours 50mg/m^2/dose on Day 1, 3 and 5. In Induction therapy II, subjects received Daunorubicin IV over 6 hours 50mg/m^2/dose on Day 1, 3 and 5.

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

Dosage and administration details:

In Induction therapy l, subjects received Etoposide IV over 4 hours 100 mg/m^2/dose from Day 1 to Day 5. In Induction therapy ll, subjects received Etoposide IV over 4 hours 100 mg/m^2/dose from Day 1 to Day 5. In Intensification therapy I, subjects received Etoposide IV over 4 hours 150 mg/m^2/dose from Day 1 to Day 5.

Number of subjects in period 1	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)
Started	531	532	6
Treated	517	520	6
Completed	304	300	3
Not completed	227	232	3
Ineligible	5	5	-
Consent withdrawn by subject	8	14	-
Other	33	43	-
Death	153	140	3
Lost to follow-up	28	30	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: No Gemtuzumab ozogamicin
Reporting group description:	
Cytarabine(ARA-C) intrathecally(IT) on Day 1 of induction therapy I,intravenous (IV) infusion (inf.) of 100 mg/m^2/twice daily ARA-C on Day 1-10; daunorubicin IV inf. of 50mg/m^2/dose on Day 1,3,5;IV inf. of 100 mg/m^2/dose etoposide on Day 1-5. After 3 weeks,ARA-C IT on Day 1 of induction therapy II,then IV ARA-C inf. of 100 mg/m^2/twice daily on Day 1-8;IV daunorubicin inf. of 50mg/m^2/dose on Day 1, 3, 5;etoposide IV infusion of 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks,ARA-C IT on Day 1 of intensification (INT) II;IV inf. of 1000 mg/m^2/twice daily of ARA-C on Day 1-4;mitoxantrone IV inf. of 12 mg/m^2/dose on Day 3-6. After 3 weeks,3 hour of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1, 2, 8, 9 of INT III and injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on basis of age.	
Reporting group title	Arm B: Gemtuzumab ozogamicin
Reporting group description:	
ARA-C (IT) on Day 1 of induction I (IND). IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-10;6 hr IV inf. daunorubicin (DAUN), 50mg/m^2/dose on Day 1,3,5; etoposide IV inf. of 100 mg/m^2/dose on Day 1-5;IV inf. of 3mg/m^2/dose of GMTZ on Day 6.After 3 weeks ARA-C IT, Day 1 of IND ll. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-8;IV inf. of 50 mg/m^2/dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m^2/dose on Day 1-5.After 3 weeks,ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m^2/twice daily of ARA-C,150 mg/m^2/dose of ETOP on Day 1-5. After 3 weeks; ARA-C IT on Day 1 of INT II; 1hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m^2/dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m^2/dose of GMTZ on Day 7. After 3 weeks of rest,3 hr of IV inf. of high dose of 3000 mg/m^2/twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m^2/dose of E. coli L-asparaginase on Day 2,9. Dose was administered on basis of age.	
Reporting group title	Arm A: No Gemtuzumab ozogamicin (Down syndrome)
Reporting group description:	
ARA-C (IT) on Day 1 of IND I. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m^2/dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy ll, then IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m^2/dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification II; a 1 hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4;1 hr IV inf. of mitoxantrone 12 mg/m^2/dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1,2,8,9 of intensification therapy III, an injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on the basis of age of the subjects.	

Reporting group values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)
Number of subjects	531	532	6
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 8.7 ± 6.4	 9.0 ± 6.2	 11.5 ± 5.5
Gender categorical Units: Subjects			
Female	260	277	4
Male	271	255	2

Reporting group values	Total		
Number of subjects	1069		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	541		
Male	528		

End points

End points reporting groups

Reporting group title	Arm A: No Gemtuzumab ozogamicin

Reporting group description:

Cytarabine(ARA-C) intrathecally(IT) on Day 1 of induction therapy I,intravenous (IV) infusion (inf.) of 100 mg/m^2/twice daily ARA-C on Day 1-10; daunorubicin IV inf. of 50mg/m^2/dose on Day 1,3,5;IV inf. of 100 mg/m^2/dose etoposide on Day 1-5. After 3 weeks,ARA-C IT on Day 1 of induction therapy II,then IV ARA-C inf. of 100 mg/m^2/twice daily on Day 1-8;IV daunorubicin inf. of 50mg/m^2/dose on Day 1, 3, 5;etoposide IV infusion of 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks,ARA-C IT on Day 1 of intensification (INT) II;IV inf. of 1000 mg/m^2/twice daily of ARA-C on Day 1-4;mitoxantrone IV inf. of 12 mg/m^2/dose on Day 3-6. After 3 weeks,3 hour of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1, 2, 8, 9 of INT III and injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on basis of age.

Reporting group title	Arm B: Gemtuzumab ozogamicin

Reporting group description:

ARA-C (IT) on Day 1 of induction I (IND). IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-10;6 hr IV inf. daunorubicin (DAUN), 50mg/m^2/dose on Day 1,3,5; etoposide IV inf. of 100 mg/m^2/dose on Day 1-5;IV inf. of 3mg/m^2/dose of GMTZ on Day 6.After 3 weeks ARA-C IT, Day 1 of IND ll. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-8;IV inf. of 50 mg/m^2/dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m^2/dose on Day 1-5.After 3 weeks,ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m^2/twice daily of ARA-C,150 mg/m^2/dose of ETOP on Day 1-5. After 3 weeks; ARA-C IT on Day 1 of INT II; 1hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m^2/dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m^2/dose of GMTZ on Day 7. After 3 weeks of rest,3 hr of IV inf. of high dose of 3000 mg/m^2/twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m^2/dose of E. coli L-asparaginase on Day 2,9. Dose was administered on basis of age.

Reporting group title	Arm A: No Gemtuzumab ozogamicin (Down syndrome)

Reporting group description:

ARA-C (IT) on Day 1 of IND I. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m^2/dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy ll, then IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m^2/dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification II; a 1 hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4;1 hr IV inf. of mitoxantrone 12 mg/m^2/dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1,2,8,9 of intensification therapy III, an injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on the basis of age of the subjects.

Primary: Event Free Survival (EFS) : Per Protocol Set

End point title	Event Free Survival (EFS) : Per Protocol Set[1]

End point description:

EFS was defined as the time from study entry until death, induction failure, or relapse of any type. The Kaplan-Meier method was used to calculate estimates of EFS. The log-rank test was used to compare survival between treatment groups. Monitoring for efficacy of GMTZ with respect to EFS utilized monitoring based on the Lan-DeMets criterion with Alpha (α) spending function αt^2 (truncated at 3 standard deviations) and 2.5% type I error. Per protocol analysis set included all randomized subjects who received at least one dose of any study treatment and were not considered ineligible as per the protocol. 99999 represents that the 95% C.I. was not reached due to immaturity of events.

End point type	Primary

End point timeframe:

Time from randomization to induction failure, relapse or death (up to 10 years)

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: The endpoint was planned to be reported for arm A: No Gemtuzumab ozogamicin and arm B: Gemtuzumab ozogamicin only.

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	511	511		
Units: Months				
median (confidence interval 95%)	18.5 (14.9 to 28.3)	54.6 (21.6 to 99999)		

Statistical analyses

Statistical analysis title	Statistical analysis of EFS
Comparison groups	Arm B: Gemtuzumab ozogamicin v Arm A: No Gemtuzumab ozogamicin
Number of subjects included in analysis	1022
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0309
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.827
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.696
upper limit	0.983

Notes:

[2] - The study was designed to have 80% power with one-sided 2.5% type I error to detect a 9% improvement in long-term EFS (54% v 45%) between the two study arms.

Primary: Event Free Survival (EFS) : Full Analysis Set

End point title	Event Free Survival (EFS) : Full Analysis Set[3]

End point description:

EFS was defined as the time from study entry until death, induction failure, or relapse of any type. The Kaplan-Meier method was used to calculate estimates of EFS. The log-rank test was used to compare survival between treatment groups. Monitoring for efficacy of GMTZ with respect to EFS utilized monitoring based on the Lan-DeMets criterion with α-spending function αt^2 (truncated at 3 standard deviations) and 2.5% type I error . Full analysis set included all randomized subjects. 99999 represents that the 95% C.I. was not reached due to immaturity of events.

End point type	Primary

End point timeframe:

Time from randomization to induction failure, relapse or death (up to 10 years)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to be reported for arm A: No Gemtuzumab ozogamicin and arm B: Gemtuzumab ozogamicin only.

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	531	532		
Units: months				
median (confidence interval 95%)	18.4 (14.9 to 28.3)	47.8 (21.1 to 99999)		

Statistical analyses

Statistical analysis title	Statistical analysis of EFS
Comparison groups	Arm A: No Gemtuzumab ozogamicin v Arm B: Gemtuzumab ozogamicin
Number of subjects included in analysis	1063
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0431
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.838
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.706
upper limit	0.995

Primary: Overall Survival (OS): Per Protocol Set

End point title	Overall Survival (OS): Per Protocol Set[4]

End point description:

OS was defined as time from randomization to the date of death due to any cause. The Kaplan-Meier method was used to calculate estimates of OS. Monitoring for efficacy of GMTZ with respect to OS utilized monitoring based on the Lan-DeMets criterion with α-spending function αt^2 (truncated at 3 standard deviations) and 2.5% type I error.
Per protocol analysis set included all randomized subjects who received at least one dose of any study treatment and were not considered ineligible as per the protocol. 99999 represents that median and 95% C.I. was not reached due to immaturity of events.

End point type	Primary

End point timeframe:

From randomization until death due to any cause (up to 10 years)

Notes:

[4] - 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: The endpoint was planned to be reported for arm A: No Gemtuzumab ozogamicin and arm B: Gemtuzumab ozogamicin only.

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	511	511		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis of OS
Comparison groups	Arm A: No Gemtuzumab ozogamicin v Arm B: Gemtuzumab ozogamicin
Number of subjects included in analysis	1022
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2638
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.879
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.103

Primary: Overall Survival (OS) : Full Analysis Set

End point title	Overall Survival (OS) : Full Analysis Set[5]

End point description:

OS was defined as time from randomization to the date of death due to any cause. The Kaplan-Meier method was used to calculate estimates of OS. Monitoring for efficacy of GMTZ with respect to OS utilized monitoring based on the Lan-DeMets criterion with α-spending function αt^2 (truncated at 3 standard deviations) and 2.5% type I error.
Full analysis set included all randomized subjects. 99999 represents that median and 95% C.I. was not reached due to immaturity of events.

End point type	Primary

End point timeframe:

From randomization until death due to any cause (up to 10 years)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The endpoint was planned to be reported for arm A: No Gemtuzumab ozogamicin and arm B: Gemtuzumab ozogamicin only.

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	531	532		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis of OS: Full analysis set
Comparison groups	Arm A: No Gemtuzumab ozogamicin v Arm B: Gemtuzumab ozogamicin
Number of subjects included in analysis	1063
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3799
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.904
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.721
upper limit	1.133

Secondary: Percentage of Subjects With Complete Remission (CR) : Full Analysis Set

End point title	Percentage of Subjects With Complete Remission (CR) : Full Analysis Set[6]

End point description:

CR was defined as percentage of subjects who had presence of < 5% blast cells and absence of extramedullary disease in the bone marrow or absence of leukemic blasts in the peripheral blood at the end of induction therapy II.
Full analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

From Randomization up to Day 56 (end of induction therapy II)

Notes:

[6] - 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: The endpoint was planned to be reported for arm A: No Gemtuzumab ozogamicin and arm B: Gemtuzumab ozogamicin only.

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	531	532		
Units: Percentage of Subjects				
number (confidence interval 95%)	76.1 (72.2 to 79.7)	78.8 (75.0 to 82.2)		

Statistical analyses

Statistical analysis title	Statistical analysis of (CR) : Full Analysis Set
Comparison groups	Arm A: No Gemtuzumab ozogamicin v Arm B: Gemtuzumab ozogamicin
Number of subjects included in analysis	1063
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3052
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	2.3

Secondary: Percentage of Subjects With Complete Remission (CR) : Per Protocol Set

End point title	Percentage of Subjects With Complete Remission (CR) : Per Protocol Set[7]

End point description:

CR was defined as percentage of subjects who had presence of < 5% blast cells and absence of extramedullary disease in the bone marrow or absence of leukemic blasts in the peripheral blood at the end of induction therapy II.
Per protocol analysis set included all randomized subjects who received at least one dose of any study treatment and were not considered ineligible as per protocol.

End point type	Secondary

End point timeframe:

From Randomization up to Day 56 (end of induction therapy II)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to be reported for arm A: No Gemtuzumab ozogamicin and arm B: Gemtuzumab ozogamicin only.

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	511	511		
Units: Percentage of Subjects				
number (confidence interval 95%)	78.7 (74.9 to 82.1)	81.6 (78.0 to 84.9)		

Statistical analyses

Statistical analysis title	Statistical analysis CR : Per Protocol Set
Comparison groups	Arm A: No Gemtuzumab ozogamicin v Arm B: Gemtuzumab ozogamicin
Number of subjects included in analysis	1022
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2723
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	2

Secondary: Disease-free Survival (DFS) : Full Analysis Set

End point title	Disease-free Survival (DFS) : Full Analysis Set

End point description:

DFS was defined as the time from the end of Intensification- I to death or relapse. Full analysis set included all randomized subjects. As specified in statistical analysis plan (SAP), due to change in planned analysis, data for disease free survival was not evaluated.

End point type	Secondary

End point timeframe:

From Day 84 (end of intensification therapy I) up to death or relapse, whichever occurred first

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[8] - Due to change in planned analysis no subject was analyzed for DFS.

[9] - Due to change in planned analysis no subject was analyzed for DFS.

[10] - Due to change in planned analysis no subject was analyzed for DFS.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-free Survival (DFS) : Per Protocol Set

End point title	Disease-free Survival (DFS) : Per Protocol Set

End point description:

DFS was defined as the time from the end of Intensification- I to death or relapse. As specified in SAP, due to change in planned analysis, data for disease free survival was not evaluated. Per protocol analysis set included all randomized subjects who received at least one dose of any study treatment and were not considered ineligible as per the protocol.

End point type	Secondary

End point timeframe:

From Day 84 (end of intensification therapy I) up to death or relapse, whichever occurred first

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[11] - Due to change in planned analysis no subject was analyzed for DFS.

[12] - Due to change in planned analysis no subject was analyzed for DFS.

[13] - Due to change in planned analysis no subject was analyzed for DFS.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Recovery of Platelets and Neutrophils

End point title	Duration of Recovery of Platelets and Neutrophils

End point description:

Time to neutrophil recovery was defined as the time from the first dose to the first date when neutrophil count was greater than 500 per milliliter (/mL). Time to platelet recovery was defined as the time from the first dose to the first date when platelet count were greater than 50,000/mL for 7 Days without transfusion. Here, 'n' subjects that were evaluable for a specified time point only. Safety analysis set included all patients who received at least 1 dose of any study treatment. 99999 represents that the 95% C.I. was not reached due to immaturity of events.

End point type	Secondary

End point timeframe:

Induction therapy I, Intensification therapy II

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	517	520	6	
Units: Days				
median (confidence interval 95%)				
Induction I : Platelets (n=517,520,6)	29.0 (28.0 to 29.0)	31.0 (30.0 to 31.0)	30.5 (19.0 to 99999)	
Induction I : Neutrophils (n=517,520,6)	33.0 (33.0 to 34.0)	33.0 (32.0 to 34.0)	29.5 (27.0 to 34.0)	
Intensification II : Platelets (n=304,326,4)	47.0 (43.0 to 51.0)	53.0 (49.0 to 59.0)	81.0 (42.0 to 99.0)	
Intensification II : Neutrophils (n=304,326,4)	40.0 (38.0 to 43.0)	42.0 (40.0 to 45.0)	54.5 (27.0 to 78.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Toxicities

End point title	Number of Subjects with Toxicities

End point description:

Number of subjects with at least one grade 3 or higher adverse event during therapy were reported in this endpoint. Safety analysis set included all subjects who received at least one dose of any study treatment.

End point type	Secondary

End point timeframe:

From first dose of study treatment up till end of study (up to 10 years)

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	517	520	6	
Units: Subjects	489	490	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Deaths

End point title	Summary of Deaths

End point description:

Safety analysis set included all subjects who received at least one dose of any study treatment.

End point type	Secondary

End point timeframe:

From first dose of study treatment through 30 Days of last dose (up to 10 years)

End point values	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	517	520	6	
Units: Subjects	15	20	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 30 Days after last dose of study treatment (up to 10 years)

Adverse event reporting additional description:

Same event may appear as an adverse event(AE) and Serious AE(i.e.only Grade 4 unexpected AEs that were related to protocol or any Grade 5 event).Events presented are distinct events.An event may be categorized as serious in one subject and as non-serious in another subject,or one subject may have experienced both SAEs and Non-SAEs during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Arm A: No Gemtuzumab ozogamicin

Reporting group description:

ARA-C (IT) on Day 1 of induction therapy I, then IV infusion of 100 mg/m^2/twice daily ARA-C on Day 1-10; daunorubicin IV infusion of 50mg/m^2/dose on Day 1,3,5; and IV inf. of 100 mg/m^2/dose etoposide on Day 1-5.After 3 weeks, ARA-C IT on Day 1 of induction therapy II,then IV ARA-C inf. of 100 mg/m^2/twice daily on Day 1-8;IV daunorubicin inf. of 50mg/m^2/dose on Day 1, 3, 5;etoposide IV infusion of 100 mg/m^2/dose on Day 1-5.After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification therapy II;IV inf. of 1000 mg/m^2/twice daily of ARA-C on Day 1-4;mitoxantrone IV inf. of 12 mg/m^2/dose on Day 3-6. After 3 weeks, 3 hour of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1, 2, 8, 9 of intensification therapy III and injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on basis of age of subjects.

Reporting group title	Arm B: Gemtuzumab ozogamicin

Reporting group description:

ARA-C (IT) on Day 1 of induction I (IND). IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-10;6 hr IV inf. daunorubicin (DAUN), 50mg/m^2/dose on Day 1,3,5; etoposide IV inf. of 100 mg/m^2/dose on Day 1-5;IV inf. of 3mg/m^2/dose of GMTZ on Day 6.After 3 weeks ARA-C IT, Day 1 of IND ll. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-8;IV inf. of 50 mg/m^2/dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m^2/dose on Day 1-5.After 3 weeks,ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m^2/twice daily of ARA-C,150 mg/m^2/dose of ETOP on Day 1-5. After 3 weeks; ARA-C IT on Day 1 of INT II; 1hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m^2/dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m^2/dose of GMTZ on Day 7. After 3 weeks of rest,3 hr of IV inf. of high dose of 3000 mg/m^2/twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m^2/dose of E. coli L-asparaginase on Day 2,9. Dose was administered on basis of age.

Reporting group title	Arm A: No Gemtuzumab ozogamicin (Down syndrome)

Reporting group description:

ARA-C (IT) on Day 1 of IND I. IV inf. of ARA-C 100 mg/m^2/twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m^2/dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy ll, then IV inf. of 100 mg/m^2/twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m^2/dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m^2/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification l and IV ARA-C inf. of 1000 mg/m^2/twice daily and 150 mg/m^2/dose of etoposide on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification II; a 1 hr IV inf. of ARA-C 1000 mg/m^2/twice daily on Day 1-4;1 hr IV inf. of mitoxantrone 12 mg/m^2/dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m^2/per day of ARA-C on Day 1,2,8,9 of intensification therapy III, an injection of E. Coli L-asparaginase 6000 IU/m^2/dose on Day 2 and 9. Dose was administered on the basis of age of the subjects.

Serious adverse events	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 517 (5.22%)	33 / 520 (6.35%)	2 / 6 (33.33%)
number of deaths (all causes)	21	23	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Second primary malignancy			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 517 (1.16%)	4 / 520 (0.77%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 6	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Venoocclusive disease			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Venous thrombosis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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			
Death			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Disease progression			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Multiple organ dysfunction syndrome			

subjects affected / exposed	6 / 517 (1.16%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 6	0 / 2	0 / 0
Sudden death			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	4 / 517 (0.77%)	7 / 520 (1.35%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Atelectasis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Bronchospasm			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Dyspnoea			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (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
Haemothorax			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypoxia			
subjects affected / exposed	7 / 517 (1.35%)	6 / 520 (1.15%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 8	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Pleural effusion			

subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (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
Pneumonitis			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Investigations			
Alanine aminotransferase			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (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
Amylase			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Aspartate aminotransferase			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine			

subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Blood fibrinogen			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Heart rate decreased			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lipase			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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			
Arrhythmia			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Cardiac arrest			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorder			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cor pulmonale			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Left ventricular dysfunction			
subjects affected / exposed	3 / 517 (0.58%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Pulseless electrical activity			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Restrictive cardiomyopathy			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Ventricular arrhythmia			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Nervous system disorders			
Central nervous system haemorrhage			

subjects affected / exposed	0 / 517 (0.00%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Encephalopathy			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Seizure			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (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
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Reflux gastritis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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

Stomatitis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Hepatitis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Hyperbilirubinaemia			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	8 / 517 (1.55%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Infections and infestations			
Anal infection			

subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Infection			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Kidney infection			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Pneumonia			
subjects affected / exposed	3 / 517 (0.58%)	3 / 520 (0.58%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Rhinitis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	12 / 517 (2.32%)	16 / 520 (3.08%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 22	0 / 0
deaths causally related to treatment / all	0 / 5	0 / 8	0 / 0
Splenic infection			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	3 / 517 (0.58%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperammonaemia			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (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
Hyperglycaemia			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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
Hypoglycaemia			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			

subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (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

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

Non-serious adverse events	Arm A: No Gemtuzumab ozogamicin	Arm B: Gemtuzumab ozogamicin	Arm A: No Gemtuzumab ozogamicin (Down syndrome)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	489 / 517 (94.58%)	490 / 520 (94.23%)	5 / 6 (83.33%)
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 517 (0.00%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Embolism			
subjects affected / exposed	3 / 517 (0.58%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	3	9	0
Haematoma			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	22 / 517 (4.26%)	38 / 520 (7.31%)	0 / 6 (0.00%)
occurrences (all)	25	42	0
Hypotension			
subjects affected / exposed	80 / 517 (15.47%)	80 / 520 (15.38%)	3 / 6 (50.00%)
occurrences (all)	102	92	4
Vasculitis			

subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Venoocclusive disease			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Brain operation			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Parenteral nutrition			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Catheter site haemorrhage			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	7 / 517 (1.35%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	8	6	0
Chills			
subjects affected / exposed	2 / 517 (0.39%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Complication associated with device			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Death			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Device related thrombosis			
subjects affected / exposed	5 / 517 (0.97%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	5	5	0
Disease progression			

subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Facial pain			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	7 / 517 (1.35%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	7	5	0
Ill-defined disorder			
subjects affected / exposed	4 / 517 (0.77%)	7 / 520 (1.35%)	0 / 6 (0.00%)
occurrences (all)	4	8	0
Localised oedema			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 517 (0.00%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Oedema			
subjects affected / exposed	3 / 517 (0.58%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Oedema peripheral			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	12 / 517 (2.32%)	10 / 520 (1.92%)	0 / 6 (0.00%)
occurrences (all)	16	10	0
Pyrexia			
subjects affected / exposed	27 / 517 (5.22%)	20 / 520 (3.85%)	0 / 6 (0.00%)
occurrences (all)	31	24	0
Systemic inflammatory response syndrome			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0

Ulcer			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Adverse drug reaction			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	25 / 517 (4.84%)	32 / 520 (6.15%)	1 / 6 (16.67%)
occurrences (all)	32	39	1
Engraftment syndrome			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Graft versus host disease			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypersensitivity			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysmenorrhoea			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ovarian failure			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pelvic pain			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Penile pain			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Perineal pain			

subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Uterine haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	2	11	0
Uterine pain			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	1	8	0
Vulvovaginal pain			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	21 / 517 (4.06%)	37 / 520 (7.12%)	0 / 6 (0.00%)
occurrences (all)	22	37	0
Apnoea			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Aspiration			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Atelectasis			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Bronchial haemorrhage			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Bronchospasm			
subjects affected / exposed	1 / 517 (0.19%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	1	5	0
Cough			

subjects affected / exposed	6 / 517 (1.16%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	6	6	0
Dyspnoea			
subjects affected / exposed	22 / 517 (4.26%)	24 / 520 (4.62%)	0 / 6 (0.00%)
occurrences (all)	26	24	0
Epistaxis			
subjects affected / exposed	16 / 517 (3.09%)	23 / 520 (4.42%)	0 / 6 (0.00%)
occurrences (all)	25	44	0
Hypoxia			
subjects affected / exposed	76 / 517 (14.70%)	84 / 520 (16.15%)	1 / 6 (16.67%)
occurrences (all)	92	96	1
Idiopathic pneumonia syndrome			
subjects affected / exposed	3 / 517 (0.58%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Laryngeal oedema			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Lung disorder			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lung infiltration			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal disorder			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Organising pneumonia			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pharyngeal haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pharyngeal inflammation			
subjects affected / exposed	5 / 517 (0.97%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	5	5	0
Pleural effusion			

subjects affected / exposed	19 / 517 (3.68%)	16 / 520 (3.08%)	0 / 6 (0.00%)
occurrences (all)	19	16	0
Pleuritic pain			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	39 / 517 (7.54%)	29 / 520 (5.58%)	0 / 6 (0.00%)
occurrences (all)	44	30	0
Pneumothorax			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pulmonary haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Pulmonary hypertension			
subjects affected / exposed	4 / 517 (0.77%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	4	3	0
Pulmonary oedema			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Respiratory disorder			
subjects affected / exposed	6 / 517 (1.16%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	6	10	0
Respiratory distress			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Respiratory failure			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Upper airway obstruction			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0

Anxiety			
subjects affected / exposed	2 / 517 (0.39%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Confusional state			
subjects affected / exposed	4 / 517 (0.77%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	4	4	0
Depression			
subjects affected / exposed	6 / 517 (1.16%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	8	3	0
Euphoric mood			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	3 / 517 (0.58%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Mental disorder			
subjects affected / exposed	6 / 517 (1.16%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	6	3	0
Personality disorder			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Investigations			
Activated partial thromboplastin time			
subjects affected / exposed	13 / 517 (2.51%)	15 / 520 (2.88%)	0 / 6 (0.00%)
occurrences (all)	13	15	0
Alanine aminotransferase			
subjects affected / exposed	84 / 517 (16.25%)	105 / 520 (20.19%)	0 / 6 (0.00%)
occurrences (all)	118	132	0
Amylase			
subjects affected / exposed	16 / 517 (3.09%)	8 / 520 (1.54%)	0 / 6 (0.00%)
occurrences (all)	17	8	0
Aspartate aminotransferase			
subjects affected / exposed	55 / 517 (10.64%)	74 / 520 (14.23%)	0 / 6 (0.00%)
occurrences (all)	62	86	0
Audiogram			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Blood creatine phosphokinase			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Blood creatinine			
subjects affected / exposed	13 / 517 (2.51%)	8 / 520 (1.54%)	0 / 6 (0.00%)
occurrences (all)	14	10	0
Blood creatinine increased			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood fibrinogen			
subjects affected / exposed	7 / 517 (1.35%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	7	3	0
Blood lactate dehydrogenase			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Coagulation test abnormal			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	71 / 517 (13.73%)	68 / 520 (13.08%)	0 / 6 (0.00%)
occurrences (all)	101	99	0
Gamma-glutamyltransferase			
subjects affected / exposed	25 / 517 (4.84%)	41 / 520 (7.88%)	0 / 6 (0.00%)
occurrences (all)	29	60	0
Glomerular filtration rate			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haemoglobin			
subjects affected / exposed	10 / 517 (1.93%)	8 / 520 (1.54%)	0 / 6 (0.00%)
occurrences (all)	14	11	0
International normalised ratio			
subjects affected / exposed	5 / 517 (0.97%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	5	5	0
Lipase			
subjects affected / exposed	27 / 517 (5.22%)	21 / 520 (4.04%)	0 / 6 (0.00%)
occurrences (all)	28	21	0
Neutrophil count			
subjects affected / exposed	15 / 517 (2.90%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	24	11	0
Neutrophil count decreased			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Platelet count			
subjects affected / exposed	13 / 517 (2.51%)	11 / 520 (2.12%)	0 / 6 (0.00%)
occurrences (all)	20	14	0
Platelet count decreased			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Protein total decreased			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Troponin I			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Troponin T			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urine analysis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Weight decreased			

subjects affected / exposed	21 / 517 (4.06%)	12 / 520 (2.31%)	0 / 6 (0.00%)
occurrences (all)	26	18	0
Weight increased			
subjects affected / exposed	16 / 517 (3.09%)	16 / 520 (3.08%)	0 / 6 (0.00%)
occurrences (all)	16	16	0
White blood cell count			
subjects affected / exposed	11 / 517 (2.13%)	8 / 520 (1.54%)	0 / 6 (0.00%)
occurrences (all)	14	10	0
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction			
subjects affected / exposed	2 / 517 (0.39%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Procedural complication			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Procedural haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Subdural haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tracheal haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Venous injury			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Wound haemorrhage			

subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Cardiac disorders			
Left ventricular dysfunction			
alternative assessment type: Systematic			
subjects affected / exposed	119 / 517 (23.02%)	106 / 520 (20.38%)	1 / 6 (16.67%)
occurrences (all)	210	196	1
Myocarditis			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pericardial effusion			
subjects affected / exposed	8 / 517 (1.55%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	8	4	0
Pericarditis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Restrictive cardiomyopathy			
subjects affected / exposed	4 / 517 (0.77%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Sinus bradycardia			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Supraventricular tachycardia			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Ventricular tachycardia			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Sinus tachycardia			
subjects affected / exposed	6 / 517 (1.16%)	10 / 520 (1.92%)	0 / 6 (0.00%)
occurrences (all)	6	12	0
Arrhythmia supraventricular			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Atrial tachycardia			

subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Atrioventricular block first degree			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cardio-respiratory arrest			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cor pulmonale			
subjects affected / exposed	3 / 517 (0.58%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Tachycardia			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	3 / 517 (0.58%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Central nervous system haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Cerebral ischaemia			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cranial nerve disorder			
subjects affected / exposed	0 / 517 (0.00%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	0	5	0
Dizziness			

subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Encephalopathy			
subjects affected / exposed	5 / 517 (0.97%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	5	5	0
Headache			
subjects affected / exposed	19 / 517 (3.68%)	27 / 520 (5.19%)	0 / 6 (0.00%)
occurrences (all)	25	35	0
Hemiparesis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hydrocephalus			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorder			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Neuralgia			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Peripheral motor neuropathy			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 517 (0.58%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	4	6	0
Seizure			
subjects affected / exposed	7 / 517 (1.35%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	7	5	0
Somnolence			
subjects affected / exposed	3 / 517 (0.58%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
Syncope			
subjects affected / exposed	5 / 517 (0.97%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	6	9	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Disseminated intravascular coagulation			
subjects affected / exposed	6 / 517 (1.16%)	13 / 520 (2.50%)	0 / 6 (0.00%)
occurrences (all)	6	13	0
Febrile neutropenia			
subjects affected / exposed	267 / 517 (51.64%)	285 / 520 (54.81%)	4 / 6 (66.67%)
occurrences (all)	505	543	8
Lymphadenopathy			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Thrombotic microangiopathy			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
External ear pain			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Conjunctival haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	1 / 517 (0.19%)	5 / 520 (0.96%)	1 / 6 (16.67%)
occurrences (all)	1	5	1
Iritis			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ocular surface disease			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Photophobia			
subjects affected / exposed	3 / 517 (0.58%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
Retinal haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Uveitis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Vitreous haemorrhage			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 517 (0.58%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
Abdominal pain			
subjects affected / exposed	38 / 517 (7.35%)	45 / 520 (8.65%)	0 / 6 (0.00%)
occurrences (all)	50	62	0
Abdominal pain upper			
subjects affected / exposed	5 / 517 (0.97%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Anal fissure			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Anal fistula			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Anal inflammation			
subjects affected / exposed	5 / 517 (0.97%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	5	4	0
Anal ulcer			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ascites			
subjects affected / exposed	18 / 517 (3.48%)	19 / 520 (3.65%)	0 / 6 (0.00%)
occurrences (all)	18	20	0
Cheilitis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Colitis			
subjects affected / exposed	42 / 517 (8.12%)	38 / 520 (7.31%)	0 / 6 (0.00%)
occurrences (all)	47	43	0
Constipation			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	80 / 517 (15.47%)	58 / 520 (11.15%)	1 / 6 (16.67%)
occurrences (all)	96	77	2
Dyspepsia			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dysphagia			
subjects affected / exposed	4 / 517 (0.77%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	4	3	0
Enteritis			
subjects affected / exposed	3 / 517 (0.58%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Gastric haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	5 / 517 (0.97%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	6	1	0

Gastrointestinal fistula			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Ileus			
subjects affected / exposed	7 / 517 (1.35%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	8	9	0
Intussusception			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Large intestinal haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lip pain			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	4 / 517 (0.77%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	4	5	0
Malabsorption			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Mouth haemorrhage			
subjects affected / exposed	4 / 517 (0.77%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	4	1	0

Nausea			
subjects affected / exposed	49 / 517 (9.48%)	62 / 520 (11.92%)	1 / 6 (16.67%)
occurrences (all)	67	84	1
Oesophageal haemorrhage			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oesophageal pain			
subjects affected / exposed	3 / 517 (0.58%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Oesophagitis			
subjects affected / exposed	12 / 517 (2.32%)	13 / 520 (2.50%)	0 / 6 (0.00%)
occurrences (all)	14	17	0
Oral pain			
subjects affected / exposed	28 / 517 (5.42%)	37 / 520 (7.12%)	0 / 6 (0.00%)
occurrences (all)	33	45	0
Pancreatitis			
subjects affected / exposed	4 / 517 (0.77%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	4	5	0
Pneumatosis intestinalis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Proctalgia			
subjects affected / exposed	19 / 517 (3.68%)	15 / 520 (2.88%)	0 / 6 (0.00%)
occurrences (all)	22	17	0
Proctitis			
subjects affected / exposed	3 / 517 (0.58%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Rectal fissure			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Rectal haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Reflux gastritis			
subjects affected / exposed	4 / 517 (0.77%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	5	4	0

Small intestinal haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Small intestinal obstruction			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Stomatitis			
subjects affected / exposed	82 / 517 (15.86%)	95 / 520 (18.27%)	2 / 6 (33.33%)
occurrences (all)	109	126	5
Tooth disorder			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	3 / 517 (0.58%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Vomiting			
subjects affected / exposed	34 / 517 (6.58%)	44 / 520 (8.46%)	0 / 6 (0.00%)
occurrences (all)	41	52	0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	4 / 517 (0.77%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	4	2	0
Gallbladder necrosis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gallbladder obstruction			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Gallbladder pain			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatic failure			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatitis			
subjects affected / exposed	6 / 517 (1.16%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	7	1	0
Hepatobiliary disease			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Hepatic pain			
subjects affected / exposed	13 / 517 (2.51%)	16 / 520 (3.08%)	0 / 6 (0.00%)
occurrences (all)	13	16	0
Hyperbilirubinaemia			
subjects affected / exposed	57 / 517 (11.03%)	60 / 520 (11.54%)	0 / 6 (0.00%)
occurrences (all)	69	70	0
Portal hypertension			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Erythema multiforme			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Exfoliative rash			
subjects affected / exposed	26 / 517 (5.03%)	30 / 520 (5.77%)	0 / 6 (0.00%)
occurrences (all)	27	34	0
Pain of skin			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Pruritus			

subjects affected / exposed	5 / 517 (0.97%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	5	4	0
Purpura			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash papular			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin disorder			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Urticaria			
subjects affected / exposed	3 / 517 (0.58%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Renal and urinary disorders			
Bladder obstruction			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bladder pain			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Proteinuria			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Renal failure			
subjects affected / exposed	11 / 517 (2.13%)	26 / 520 (5.00%)	1 / 6 (16.67%)
occurrences (all)	11	26	1
Renal necrosis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Renal pain			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ureteric stenosis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urethral pain			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urinary bladder haemorrhage			
subjects affected / exposed	2 / 517 (0.39%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Urogenital haemorrhage			
subjects affected / exposed	1 / 517 (0.19%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	1	5	0
Endocrine disorders			
Diabetes insipidus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Adrenal insufficiency			
subjects affected / exposed	0 / 517 (0.00%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 517 (0.58%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	4	2	0
Arthritis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	14 / 517 (2.71%)	11 / 520 (2.12%)	0 / 6 (0.00%)
occurrences (all)	16	14	0
Bone infarction			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Bone pain			
subjects affected / exposed	2 / 517 (0.39%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Cytarabine syndrome			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Joint effusion			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Muscular weakness			
subjects affected / exposed	3 / 517 (0.58%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	4	3	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 517 (0.00%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal disorder			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 517 (0.39%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	2	5	0
Myalgia			
subjects affected / exposed	1 / 517 (0.19%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	1	6	0
Myositis			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Neck pain			
subjects affected / exposed	2 / 517 (0.39%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Osteonecrosis			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	14 / 517 (2.71%)	18 / 520 (3.46%)	0 / 6 (0.00%)
occurrences (all)	19	19	0

Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 517 (0.19%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	1	7	0
Anal infection			
subjects affected / exposed	8 / 517 (1.55%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	8	10	0
Anorectal infection			
subjects affected / exposed	5 / 517 (0.97%)	10 / 520 (1.92%)	0 / 6 (0.00%)
occurrences (all)	6	11	0
Appendicitis			
subjects affected / exposed	9 / 517 (1.74%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	9	6	0
Arthritis infective			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Biliary tract infection			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Bronchitis			
subjects affected / exposed	7 / 517 (1.35%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	7	9	0
Cellulitis			
subjects affected / exposed	61 / 517 (11.80%)	43 / 520 (8.27%)	1 / 6 (16.67%)
occurrences (all)	66	49	1
Cholecystitis infective			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Clostridium difficile colitis			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Corneal infection			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	15 / 517 (2.90%)	19 / 520 (3.65%)	0 / 6 (0.00%)
occurrences (all)	25	24	0
Device related infection			
subjects affected / exposed	4 / 517 (0.77%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	4	6	0
Encephalitis			
subjects affected / exposed	6 / 517 (1.16%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	6	2	0
Endocarditis			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Enteritis infectious			
subjects affected / exposed	10 / 517 (1.93%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	13	6	0
Enterococcal infection			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	2 / 517 (0.39%)	8 / 520 (1.54%)	0 / 6 (0.00%)
occurrences (all)	2	8	0
Fungal infection			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastric infection			
subjects affected / exposed	4 / 517 (0.77%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	11 / 517 (2.13%)	13 / 520 (2.50%)	0 / 6 (0.00%)
occurrences (all)	13	14	0
Herpes simplex			

subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	20 / 517 (3.87%)	24 / 520 (4.62%)	0 / 6 (0.00%)
occurrences (all)	22	26	0
Infectious colitis			
subjects affected / exposed	95 / 517 (18.38%)	75 / 520 (14.42%)	0 / 6 (0.00%)
occurrences (all)	142	89	0
Infective myositis			
subjects affected / exposed	3 / 517 (0.58%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Kidney infection			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Lip infection			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lymphangitis			
subjects affected / exposed	2 / 517 (0.39%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	2	6	0
Mediastinitis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Meningitis			
subjects affected / exposed	3 / 517 (0.58%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
Mucosal infection			
subjects affected / exposed	5 / 517 (0.97%)	10 / 520 (1.92%)	0 / 6 (0.00%)
occurrences (all)	6	14	0
Nail infection			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Neutropenic infection			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oesophageal infection			

subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Opportunistic infection			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	11 / 517 (2.13%)	16 / 520 (3.08%)	0 / 6 (0.00%)
occurrences (all)	11	17	0
Oral herpes			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Osteomyelitis			
subjects affected / exposed	2 / 517 (0.39%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Otitis externa			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Otitis media			
subjects affected / exposed	6 / 517 (1.16%)	5 / 520 (0.96%)	1 / 6 (16.67%)
occurrences (all)	6	5	1
Penile infection			
subjects affected / exposed	0 / 517 (0.00%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Periorbital cellulitis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Peritonitis			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	4 / 517 (0.77%)	7 / 520 (1.35%)	0 / 6 (0.00%)
occurrences (all)	4	7	0
Pneumonia			
subjects affected / exposed	101 / 517 (19.54%)	92 / 520 (17.69%)	0 / 6 (0.00%)
occurrences (all)	131	107	0
Pseudomembranous colitis			

subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pulmonary mycosis			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	15 / 517 (2.90%)	11 / 520 (2.12%)	0 / 6 (0.00%)
occurrences (all)	19	11	0
Scrotal infection			
subjects affected / exposed	0 / 517 (0.00%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Sepsis			
subjects affected / exposed	361 / 517 (69.83%)	374 / 520 (71.92%)	4 / 6 (66.67%)
occurrences (all)	887	920	11
Sialoadenitis			
subjects affected / exposed	2 / 517 (0.39%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Sinusitis			
subjects affected / exposed	13 / 517 (2.51%)	22 / 520 (4.23%)	0 / 6 (0.00%)
occurrences (all)	13	28	0
Soft tissue infection			
subjects affected / exposed	8 / 517 (1.55%)	8 / 520 (1.54%)	0 / 6 (0.00%)
occurrences (all)	8	11	0
Splenic infection			
subjects affected / exposed	1 / 517 (0.19%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Tooth infection			
subjects affected / exposed	3 / 517 (0.58%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	3	3	0
Tracheitis			
subjects affected / exposed	4 / 517 (0.77%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	8	7	0
Upper aerodigestive tract infection			
subjects affected / exposed	1 / 517 (0.19%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Upper respiratory tract infection			

subjects affected / exposed	23 / 517 (4.45%)	24 / 520 (4.62%)	1 / 6 (16.67%)
occurrences (all)	24	30	1
Urinary tract infection			
subjects affected / exposed	35 / 517 (6.77%)	31 / 520 (5.96%)	0 / 6 (0.00%)
occurrences (all)	50	35	0
Uterine infection			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	2 / 517 (0.39%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Vulvitis			
subjects affected / exposed	7 / 517 (1.35%)	3 / 520 (0.58%)	0 / 6 (0.00%)
occurrences (all)	8	3	0
Wound infection			
subjects affected / exposed	12 / 517 (2.32%)	13 / 520 (2.50%)	0 / 6 (0.00%)
occurrences (all)	17	14	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	7 / 517 (1.35%)	12 / 520 (2.31%)	0 / 6 (0.00%)
occurrences (all)	7	13	0
Alkalosis			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Decreased appetite			
subjects affected / exposed	144 / 517 (27.85%)	166 / 520 (31.92%)	2 / 6 (33.33%)
occurrences (all)	228	290	2
Dehydration			
subjects affected / exposed	16 / 517 (3.09%)	16 / 520 (3.08%)	0 / 6 (0.00%)
occurrences (all)	17	18	0
Diabetes mellitus			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Hypercalcaemia			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0

Hyperglycaemia			
subjects affected / exposed	117 / 517 (22.63%)	126 / 520 (24.23%)	1 / 6 (16.67%)
occurrences (all)	153	153	1
Hyperkalaemia			
subjects affected / exposed	25 / 517 (4.84%)	41 / 520 (7.88%)	1 / 6 (16.67%)
occurrences (all)	28	46	1
Hypermagnesaemia			
subjects affected / exposed	5 / 517 (0.97%)	14 / 520 (2.69%)	0 / 6 (0.00%)
occurrences (all)	5	15	0
Hypernatraemia			
subjects affected / exposed	7 / 517 (1.35%)	16 / 520 (3.08%)	1 / 6 (16.67%)
occurrences (all)	7	17	1
Hyperphosphataemia			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	3 / 517 (0.58%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	3	6	0
Hyperuricaemia			
subjects affected / exposed	2 / 517 (0.39%)	7 / 520 (1.35%)	0 / 6 (0.00%)
occurrences (all)	2	7	0
Hypoalbuminaemia			
subjects affected / exposed	24 / 517 (4.64%)	25 / 520 (4.81%)	0 / 6 (0.00%)
occurrences (all)	26	26	0
Hypocalcaemia			
subjects affected / exposed	55 / 517 (10.64%)	45 / 520 (8.65%)	1 / 6 (16.67%)
occurrences (all)	62	51	1
Hypoglycaemia			
subjects affected / exposed	3 / 517 (0.58%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
Hypokalaemia			
subjects affected / exposed	169 / 517 (32.69%)	191 / 520 (36.73%)	1 / 6 (16.67%)
occurrences (all)	261	299	1
Hypomagnesaemia			
subjects affected / exposed	17 / 517 (3.29%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	20	10	0

Hyponatraemia			
subjects affected / exposed	59 / 517 (11.41%)	65 / 520 (12.50%)	1 / 6 (16.67%)
occurrences (all)	71	70	1
Hypophagia			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
subjects affected / exposed	43 / 517 (8.32%)	58 / 520 (11.15%)	0 / 6 (0.00%)
occurrences (all)	52	65	0
Tumour lysis syndrome			
subjects affected / exposed	9 / 517 (1.74%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	9	9	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25092781