

**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
<b>Arm title</b>	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<sup>2</sup>/twice daily ARA-C on Day 1-10; daunorubicin IV inf. of 50mg/m<sup>2</sup>/dose on Day 1,3,5;IV inf. of 100 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-8;IV daunorubicin inf. of 50mg/m<sup>2</sup>/dose on Day 1, 3, 5;etoposide IV infusion of 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m<sup>2</sup>/twice daily and 150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily of ARA-C on Day 1-4;mitoxantrone IV inf. of 12 mg/m<sup>2</sup>/dose on Day 3-6. After 3 weeks,3 hour of IV inf. of high dose of 3000 mg/m<sup>2</sup>/per day of ARA-C on Day 1, 2, 8, 9 of INT III and injection of E. Coli L-asparaginase 6000 IU/m<sup>2</sup>/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 I, subjects received ARA-C (IT) at on Day 1 followed by an IV infusion of 100 mg/m<sup>2</sup>/twice daily on Day 1-10. In Induction therapy II, subjects received ARA-C (IT) on Day 1 followed by an IV infusion of 100 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-5. In intensification therapy II, subjects received ARA-C (IT) followed by an IV infusion of 1000 mg/m<sup>2</sup>/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<sup>2</sup>/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 I, subjects received Daunorubicin IV over 6 hours 50mg/m<sup>2</sup>/dose on Day 1,3 and 5. In Induction therapy II, subjects received Daunorubicin IV over 6 hours 50mg/m<sup>2</sup>/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 I, subjects received etoposide IV over 4 hours 100 mg/m<sup>2</sup>/dose from Day 1 to Day 5. In Induction therapy II, subjects received Etoposide IV over 4 hours 100 mg/m<sup>2</sup>/dose from Day 1 to Day 5. In Intensification therapy I subjects received etoposide IV over 4 hours 150 mg/m<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/dose on Day 2 and 9.

<b>Arm title</b>	Arm B: Gemtuzumab ozogamicin
------------------	------------------------------

Arm description:

ARA-C (IT) on Day 1 of induction I (IND). IV inf. of 100 mg/m<sup>2</sup>/twice daily of ARA-C on Day 1-10; 6 hr IV inf. daunorubicin (DAUN), 50mg/m<sup>2</sup>/dose on Day 1,3,5; etoposide IV inf. of 100 mg/m<sup>2</sup>/dose on Day 1-5; IV inf. of 3mg/m<sup>2</sup>/dose of GMTZ on Day 6. After 3 weeks ARA-C IT, Day 1 of IND II. IV inf. of ARA-C 100 mg/m<sup>2</sup>/twice daily on Day 1-8; IV inf. of 50 mg/m<sup>2</sup>/dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m<sup>2</sup>/twice daily of ARA-C, 150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m<sup>2</sup>/dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m<sup>2</sup>/dose of GMTZ on Day 7. After 3 weeks of rest, 3 hr of IV inf. of high dose of 3000 mg/m<sup>2</sup>/twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m<sup>2</sup>/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 I, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m<sup>2</sup>/twice daily on Day 1-10. In Induction therapy II, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-5. In intensification therapy II, subjects received ARA-C intrathecally followed by an IV infusion

of 1000 mg/m<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/dose on Day 1,3 and 5. In Induction therapy II, subjects received Daunorubicin IV over 6 hours 50 mg/m<sup>2</sup>/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 I, subjects received Etoposide IV over 4 hours 100 mg/m<sup>2</sup>/dose from Day 1 to Day 5. In Induction therapy II, subjects received Etoposide IV over 4 hours 100 mg/m<sup>2</sup>/dose from Day 1 to Day 5. In Intensification therapy I subjects received Etoposide IV over 4 hours 150 mg/m<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/dose at Day 6. In Intensification therapy II, subjects received Gemtuzumab Ozogamicin IV over 2 hours 3mg/m<sup>2</sup>/dose at Day 7.

<b>Arm title</b>	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<sup>2</sup>/twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m<sup>2</sup>/dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy II, then IV inf. of 100 mg/m<sup>2</sup>/twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m<sup>2</sup>/dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m<sup>2</sup>/twice daily and 150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-4; 1 hr IV inf. of mitoxantrone 12 mg/m<sup>2</sup>/dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m<sup>2</sup>/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<sup>2</sup>/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 I, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m<sup>2</sup>/twice daily on Day 1-10. In Induction therapy II, subjects received ARA-C intrathecally on Day 1 followed by an IV infusion of 100 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-5. In intensification therapy II, subjects received ARA-C intrathecally followed by an IV infusion of 1000 mg/m<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/dose on Day 1, 3 and 5. In Induction therapy II, subjects received Daunorubicin IV over 6 hours 50mg/m<sup>2</sup>/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 I, subjects received Etoposide IV over 4 hours 100 mg/m<sup>2</sup>/dose from Day 1 to Day 5. In Induction therapy II, subjects received Etoposide IV over 4 hours 100 mg/m<sup>2</sup>/dose from Day 1 to Day 5. In Intensification therapy I, subjects received Etoposide IV over 4 hours 150 mg/m<sup>2</sup>/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 <sup>2</sup> /twice daily ARA-C on Day 1-10; daunorubicin IV inf. of 50mg/m <sup>2</sup> /dose on Day 1,3,5; IV inf. of 100 mg/m <sup>2</sup> /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 <sup>2</sup> /twice daily on Day 1-8; IV daunorubicin inf. of 50mg/m <sup>2</sup> /dose on Day 1, 3, 5; etoposide IV infusion of 100 mg/m <sup>2</sup> /dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m <sup>2</sup> /twice daily and 150 mg/m <sup>2</sup> /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 <sup>2</sup> /twice daily of ARA-C on Day 1-4; mitoxantrone IV inf. of 12 mg/m <sup>2</sup> /dose on Day 3-6. After 3 weeks, 3 hour of IV inf. of high dose of 3000 mg/m <sup>2</sup> /per day of ARA-C on Day 1, 2, 8, 9 of INT III and injection of E. Coli L-asparaginase 6000 IU/m <sup>2</sup> /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 <sup>2</sup> /twice daily of ARA-C on Day 1-10; 6 hr IV inf. daunorubicin (DAUN), 50mg/m <sup>2</sup> /dose on Day 1,3,5; etoposide IV inf. of 100 mg/m <sup>2</sup> /dose on Day 1-5; IV inf. of 3mg/m <sup>2</sup> /dose of GMTZ on Day 6. After 3 weeks ARA-C IT, Day 1 of IND II. IV inf. of ARA-C 100 mg/m <sup>2</sup> /twice daily on Day 1-8; IV inf. of 50 mg/m <sup>2</sup> /dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m <sup>2</sup> /dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m <sup>2</sup> /twice daily of ARA-C, 150 mg/m <sup>2</sup> /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 <sup>2</sup> /twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m <sup>2</sup> /dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m <sup>2</sup> /dose of GMTZ on Day 7. After 3 weeks of rest, 3 hr of IV inf. of high dose of 3000 mg/m <sup>2</sup> /twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m <sup>2</sup> /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 <sup>2</sup> /twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m <sup>2</sup> /dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m <sup>2</sup> /dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy II, then IV inf. of 100 mg/m <sup>2</sup> /twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m <sup>2</sup> /dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m <sup>2</sup> /dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m <sup>2</sup> /twice daily and 150 mg/m <sup>2</sup> /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 <sup>2</sup> /twice daily on Day 1-4; 1 hr IV inf. of mitoxantrone 12 mg/m <sup>2</sup> /dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m <sup>2</sup> /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 <sup>2</sup> /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

<b>Reporting group values</b>	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<sup>2</sup>/twice daily ARA-C on Day 1-10; daunorubicin IV inf. of 50mg/m<sup>2</sup>/dose on Day 1,3,5;IV inf. of 100 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-8;IV daunorubicin inf. of 50mg/m<sup>2</sup>/dose on Day 1, 3, 5;etoposide IV infusion of 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m<sup>2</sup>/twice daily and 150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily of ARA-C on Day 1-4;mitoxantrone IV inf. of 12 mg/m<sup>2</sup>/dose on Day 3-6. After 3 weeks,3 hour of IV inf. of high dose of 3000 mg/m<sup>2</sup>/per day of ARA-C on Day 1, 2, 8, 9 of INT III and injection of E. Coli L-asparaginase 6000 IU/m<sup>2</sup>/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<sup>2</sup>/twice daily of ARA-C on Day 1-10;6 hr IV inf. daunorubicin (DAUN), 50mg/m<sup>2</sup>/dose on Day 1,3,5; etoposide IV inf. of 100 mg/m<sup>2</sup>/dose on Day 1-5;IV inf. of 3mg/m<sup>2</sup>/dose of GMTZ on Day 6.After 3 weeks ARA-C IT, Day 1 of IND II. IV inf. of ARA-C 100 mg/m<sup>2</sup>/twice daily on Day 1-8;IV inf. of 50 mg/m<sup>2</sup>/dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m<sup>2</sup>/dose on Day 1-5.After 3 weeks,ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m<sup>2</sup>/twice daily of ARA-C,150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m<sup>2</sup>/dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m<sup>2</sup>/dose of GMTZ on Day 7. After 3 weeks of rest,3 hr of IV inf. of high dose of 3000 mg/m<sup>2</sup>/twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m<sup>2</sup>/dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy II, then IV inf. of 100 mg/m<sup>2</sup>/twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m<sup>2</sup>/dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m<sup>2</sup>/twice daily and 150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-4;1 hr IV inf. of mitoxantrone 12 mg/m<sup>2</sup>/dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m<sup>2</sup>/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<sup>2</sup>/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 <sup>[1]</sup>
-----------------	---

#### 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 ( $\alpha$ ) spending function at<sup>2</sup> (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.

<b>End point values</b>	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

<b>Statistical analysis title</b>	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 <sup>[2]</sup>
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 <sup>[3]</sup>
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 $\alpha$ -spending function at <sup>2</sup> (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.

<b>End point values</b>	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

<b>Statistical analysis title</b>	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 <sup>[4]</sup>
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 $\alpha$ -spending function at $\alpha^2$ (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.

<b>End point values</b>	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

<b>Statistical analysis title</b>	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 <sup>[5]</sup>
End point description:	<p>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 <math>\alpha</math>-spending function at<sup>2</sup> (truncated at 3 standard deviations) and 2.5% type I error.</p> <p>Full analysis set included all randomized subjects. 99999 represents that median and 95% C.I. was not reached due to immaturity of events.</p>
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.

<b>End point values</b>	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

<b>Statistical analysis title</b>	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 <sup>[6]</sup>
-----------------	--

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.

<b>End point values</b>	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

<b>Statistical analysis title</b>	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 <sup>[7]</sup>
-----------------	---

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.

<b>End point values</b>	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

<b>Statistical analysis title</b>	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

<b>End point values</b>	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 <sup>[8]</sup>	0 <sup>[9]</sup>	0 <sup>[10]</sup>	
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 <sup>[11]</sup>	0 <sup>[12]</sup>	0 <sup>[13]</sup>	
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

<b>End point values</b>	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)	

<b>End point values</b>	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)

---

<b>End point values</b>	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<sup>2</sup>/twice daily ARA-C on Day 1-10; daunorubicin IV infusion of 50mg/m<sup>2</sup>/dose on Day 1,3,5; and IV inf. of 100 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-8;IV daunorubicin inf. of 50mg/m<sup>2</sup>/dose on Day 1, 3, 5;etoposide IV infusion of 100 mg/m<sup>2</sup>/dose on Day 1-5.After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m<sup>2</sup>/twice daily and 150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily of ARA-C on Day 1-4;mitoxantrone IV inf. of 12 mg/m<sup>2</sup>/dose on Day 3-6. After 3 weeks, 3 hour of IV inf. of high dose of 3000 mg/m<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/twice daily of ARA-C on Day 1-10;6 hr IV inf. daunorubicin (DAUN), 50mg/m<sup>2</sup>/dose on Day 1,3,5; etoposide IV inf. of 100 mg/m<sup>2</sup>/dose on Day 1-5;IV inf. of 3mg/m<sup>2</sup>/dose of GMTZ on Day 6.After 3 weeks ARA-C IT, Day 1 of IND II. IV inf. of ARA-C 100 mg/m<sup>2</sup>/twice daily on Day 1-8;IV inf. of 50 mg/m<sup>2</sup>/dose of DAUN on Day 1,3,5; IV inf. of etoposide (ETOP) of 100 mg/m<sup>2</sup>/dose on Day 1-5.After 3 weeks,ARA-C IT on Day 1 of INT I, IV inf. of 1000 mg/m<sup>2</sup>/twice daily of ARA-C,150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-4; 1 hr IV inf. of 12 mg/m<sup>2</sup>/dose of mitoxantrone on Day 3-6. 2 hr inf. of 3mg/m<sup>2</sup>/dose of GMTZ on Day 7. After 3 weeks of rest,3 hr of IV inf. of high dose of 3000 mg/m<sup>2</sup>/twice daily of ARA-C on Day 1,2,8,9 of INT III and an injection of 6000 IU/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-10; a 6 hr IV inf. DAUN 50mg/m<sup>2</sup>/dose on Day 1, 3,5; 4-hr IV inf. of etoposide 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of induction therapy II, then IV inf. of 100 mg/m<sup>2</sup>/twice daily of ARA-C on Day 1-8; 6-hr IV inf. of 50mg/m<sup>2</sup>/dose of DAUN on Day 1,3,5; a 4 hr IV inf. of etoposide 100 mg/m<sup>2</sup>/dose on Day 1-5. After 3 weeks, ARA-C IT on Day 1 of intensification I and IV ARA-C inf. of 1000 mg/m<sup>2</sup>/twice daily and 150 mg/m<sup>2</sup>/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<sup>2</sup>/twice daily on Day 1-4;1 hr IV inf. of mitoxantrone 12 mg/m<sup>2</sup>/dose on Day 3-6. After 3 weeks, 3 hr of IV inf. of high dose of 3000 mg/m<sup>2</sup>/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<sup>2</sup>/dose on Day 2 and 9. Dose was administered on the basis of age of the subjects.

---

<b>Serious adverse events</b>	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
Venocclusive 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
<b>Sudden death</b>			
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
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>Acute respiratory distress syndrome</b>			
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
<b>Atelectasis</b>			
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
<b>Bronchospasm</b>			
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
<b>Dyspnoea</b>			
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
<b>Haemothorax</b>			
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
<b>Hypoxia</b>			
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
<b>Pleural effusion</b>			

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
<b>Pneumonitis</b>			
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
<b>Pulmonary haemorrhage</b>			
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
<b>Pulmonary oedema</b>			
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
<b>Respiratory failure</b>			
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
<b>Investigations</b>			
<b>Alanine aminotransferase</b>			
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
<b>Amylase</b>			
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
<b>Aspartate aminotransferase</b>			
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
<b>Blood creatinine</b>			

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
<b>Blood fibrinogen</b>			
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
<b>Electrocardiogram QT prolonged</b>			
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
<b>Heart rate decreased</b>			
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
<b>Lipase</b>			
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
<b>Cardiac disorders</b>			
<b>Arrhythmia</b>			
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
<b>Atrial flutter</b>			
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
<b>Cardiac arrest</b>			
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
<b>Cardiac disorder</b>			

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
<b>Cerebral ischaemia</b>			
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
<b>Encephalopathy</b>			
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
<b>Seizure</b>			
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
<b>Blood and lymphatic system disorders</b>			
<b>Disseminated intravascular coagulation</b>			
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
<b>Febrile neutropenia</b>			
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
<b>Gastrointestinal disorders</b>			
<b>Ascites</b>			
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
<b>Reflux gastritis</b>			
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
<b>Infection</b>			
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
<b>Infectious colitis</b>			
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
<b>Kidney infection</b>			
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
<b>Otitis media</b>			
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
<b>Pneumonia</b>			
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
<b>Rhinitis</b>			
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
<b>Sepsis</b>			
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
<b>Splenic infection</b>			

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 %

<b>Non-serious adverse events</b>	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 occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Venoocclusive disease subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Surgical and medical procedures Brain operation subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Parenteral nutrition subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions Catheter site haemorrhage subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	7 / 517 (1.35%) 8	6 / 520 (1.15%) 6	0 / 6 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	3 / 520 (0.58%) 3	0 / 6 (0.00%) 0
Complication associated with device subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Death subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Device related thrombosis subjects affected / exposed occurrences (all)	5 / 517 (0.97%) 5	5 / 520 (0.96%) 5	0 / 6 (0.00%) 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 occurrences (all)	2 / 517 (0.39%) 2	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Adverse drug reaction subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Immune system disorders			
Drug hypersensitivity subjects affected / exposed occurrences (all)	25 / 517 (4.84%) 32	32 / 520 (6.15%) 39	1 / 6 (16.67%) 1
Engraftment syndrome subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Graft versus host disease subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Hypersensitivity subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	1 / 6 (16.67%) 1
Reproductive system and breast disorders			
Balanoposthitis subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Ovarian failure subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Penile pain subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	2 / 520 (0.38%) 2	0 / 6 (0.00%) 0
Perineal pain			

subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	4 / 520 (0.77%) 4	0 / 6 (0.00%) 0
Uterine haemorrhage subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	6 / 520 (1.15%) 11	0 / 6 (0.00%) 0
Uterine pain subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	6 / 520 (1.15%) 8	0 / 6 (0.00%) 0
Vulvovaginal pain subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome subjects affected / exposed occurrences (all)	21 / 517 (4.06%) 22	37 / 520 (7.12%) 37	0 / 6 (0.00%) 0
Apnoea subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Aspiration subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	2 / 520 (0.38%) 2	0 / 6 (0.00%) 0
Atelectasis subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Bronchial haemorrhage subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Bronchospasm subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	4 / 520 (0.77%) 5	0 / 6 (0.00%) 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 occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Blood alkaline phosphatase subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	2 / 520 (0.38%) 2	0 / 6 (0.00%) 0
Blood bicarbonate decreased subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Blood creatine phosphokinase subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 2	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Blood creatinine subjects affected / exposed occurrences (all)	13 / 517 (2.51%) 14	8 / 520 (1.54%) 10	0 / 6 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Blood fibrinogen subjects affected / exposed occurrences (all)	7 / 517 (1.35%) 7	3 / 520 (0.58%) 3	0 / 6 (0.00%) 0
Blood lactate dehydrogenase subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Coagulation test abnormal subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	71 / 517 (13.73%) 101	68 / 520 (13.08%) 99	0 / 6 (0.00%) 0
Gamma-glutamyltransferase subjects affected / exposed occurrences (all)	25 / 517 (4.84%) 29	41 / 520 (7.88%) 60	0 / 6 (0.00%) 0
Glomerular filtration rate			

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

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

subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Cardiac disorders			
Left ventricular dysfunction alternative assessment type: Systematic			
subjects affected / exposed occurrences (all)	119 / 517 (23.02%) 210	106 / 520 (20.38%) 196	1 / 6 (16.67%) 1
Myocarditis			
subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Pericardial effusion			
subjects affected / exposed occurrences (all)	8 / 517 (1.55%) 8	4 / 520 (0.77%) 4	0 / 6 (0.00%) 0
Pericarditis			
subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Restrictive cardiomyopathy			
subjects affected / exposed occurrences (all)	4 / 517 (0.77%) 4	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Sinus bradycardia			
subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Supraventricular tachycardia			
subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Ventricular tachycardia			
subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	4 / 520 (0.77%) 4	0 / 6 (0.00%) 0
Sinus tachycardia			
subjects affected / exposed occurrences (all)	6 / 517 (1.16%) 6	10 / 520 (1.92%) 12	0 / 6 (0.00%) 0
Arrhythmia supraventricular			
subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 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
<b>Encephalopathy</b>			
subjects affected / exposed	5 / 517 (0.97%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	5	5	0
<b>Headache</b>			
subjects affected / exposed	19 / 517 (3.68%)	27 / 520 (5.19%)	0 / 6 (0.00%)
occurrences (all)	25	35	0
<b>Hemiparesis</b>			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
<b>Hydrocephalus</b>			
subjects affected / exposed	1 / 517 (0.19%)	0 / 520 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
<b>Nervous system disorder</b>			
subjects affected / exposed	1 / 517 (0.19%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
<b>Neuralgia</b>			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
<b>Peripheral motor neuropathy</b>			
subjects affected / exposed	2 / 517 (0.39%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
<b>Peripheral sensory neuropathy</b>			
subjects affected / exposed	3 / 517 (0.58%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	4	6	0
<b>Seizure</b>			
subjects affected / exposed	7 / 517 (1.35%)	5 / 520 (0.96%)	0 / 6 (0.00%)
occurrences (all)	7	5	0
<b>Somnolence</b>			
subjects affected / exposed	3 / 517 (0.58%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
<b>Syncope</b>			
subjects affected / exposed	5 / 517 (0.97%)	9 / 520 (1.73%)	0 / 6 (0.00%)
occurrences (all)	6	9	0
<b>Blood and lymphatic system disorders</b>			

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 occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Ocular surface disease subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Photophobia subjects affected / exposed occurrences (all)	3 / 517 (0.58%) 3	4 / 520 (0.77%) 4	0 / 6 (0.00%) 0
Retinal haemorrhage subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Uveitis subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	2 / 520 (0.38%) 2	0 / 6 (0.00%) 0
Vitreous haemorrhage subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
<b>Gastrointestinal disorders</b>			
Abdominal distension subjects affected / exposed occurrences (all)	3 / 517 (0.58%) 3	4 / 520 (0.77%) 4	0 / 6 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	38 / 517 (7.35%) 50	45 / 520 (8.65%) 62	0 / 6 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 517 (0.97%) 5	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Anal fissure subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Anal fistula subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 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
Gastroesophageal 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 occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Small intestinal obstruction subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	82 / 517 (15.86%) 109	95 / 520 (18.27%) 126	2 / 6 (33.33%) 5
Tooth disorder subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	3 / 517 (0.58%) 3	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Upper gastrointestinal haemorrhage subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	3 / 520 (0.58%) 3	0 / 6 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	34 / 517 (6.58%) 41	44 / 520 (8.46%) 52	0 / 6 (0.00%) 0
Hepatobiliary disorders			
Cholecystitis subjects affected / exposed occurrences (all)	4 / 517 (0.77%) 4	2 / 520 (0.38%) 2	0 / 6 (0.00%) 0
Gallbladder necrosis subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Gallbladder obstruction subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Gallbladder pain subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Hepatic failure			

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

subjects affected / exposed occurrences (all)	5 / 517 (0.97%) 5	4 / 520 (0.77%) 4	0 / 6 (0.00%) 0
Purpura subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Rash papular subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Skin disorder subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	2 / 520 (0.38%) 2	0 / 6 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	3 / 517 (0.58%) 3	2 / 520 (0.38%) 2	0 / 6 (0.00%) 0
Renal and urinary disorders			
Bladder obstruction subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 0
Bladder pain subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Micturition urgency subjects affected / exposed occurrences (all)	0 / 517 (0.00%) 0	1 / 520 (0.19%) 2	0 / 6 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	2 / 517 (0.39%) 2	1 / 520 (0.19%) 1	0 / 6 (0.00%) 0
Renal failure subjects affected / exposed occurrences (all)	11 / 517 (2.13%) 11	26 / 520 (5.00%) 26	1 / 6 (16.67%) 1
Renal necrosis subjects affected / exposed occurrences (all)	1 / 517 (0.19%) 1	0 / 520 (0.00%) 0	0 / 6 (0.00%) 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
<b>Infection</b>			
subjects affected / exposed	20 / 517 (3.87%)	24 / 520 (4.62%)	0 / 6 (0.00%)
occurrences (all)	22	26	0
<b>Infectious colitis</b>			
subjects affected / exposed	95 / 517 (18.38%)	75 / 520 (14.42%)	0 / 6 (0.00%)
occurrences (all)	142	89	0
<b>Infective myositis</b>			
subjects affected / exposed	3 / 517 (0.58%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
<b>Kidney infection</b>			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
<b>Lip infection</b>			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
<b>Lymphangitis</b>			
subjects affected / exposed	2 / 517 (0.39%)	6 / 520 (1.15%)	0 / 6 (0.00%)
occurrences (all)	2	6	0
<b>Mediastinitis</b>			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
<b>Meningitis</b>			
subjects affected / exposed	3 / 517 (0.58%)	4 / 520 (0.77%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
<b>Mucosal infection</b>			
subjects affected / exposed	5 / 517 (0.97%)	10 / 520 (1.92%)	0 / 6 (0.00%)
occurrences (all)	6	14	0
<b>Nail infection</b>			
subjects affected / exposed	1 / 517 (0.19%)	2 / 520 (0.38%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
<b>Neutropenic infection</b>			
subjects affected / exposed	0 / 517 (0.00%)	1 / 520 (0.19%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
<b>Oesophageal infection</b>			

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>