Clinical trial results:
Randomized phase-II trial evaluating induction therapy with idarubicin and etoposide plus sequential or concurrent azacitidine and maintenance therapy with azacitidine

Summary

EudraCT number	2009-016142-44
Trial protocol	DE AT
Global end of trial date	02 October 2016

Results information

Result version number	v1 (current)
This version publication date	22 October 2017
First version publication date	22 October 2017

Trial information

Trial identification

Sponsor protocol code	AMLSG 12-09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01180322
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital of Ulm
Sponsor organisation address	Albert-Einstein-Allee 23, Ulm, Germany, 89081
Public contact	Prof. Dr. Richard Schlenk, University Hospital of Ulm, 0049 73150045980, richard.schlenk@nct-heidelberg.de
Scientific contact	Prof. Dr. Richard Schlenk, University Hospital of Ulm, 0049 73150045980, richard.schlenk@nct-heidelberg.de

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 October 2016
Global end of trial reached?	Yes
Global end of trial date	02 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Efficacy Objective
- To evaluate the impact of sequential or concurrent addition of 5-azacytidine to intensive induction chemotherapy with idarubicin and etoposide on the CR rate

Secondary Efficacy Objectives
- To evaluate the impact of sequential or concurrent addition of 5-azacytidine to intensive induction chemotherapy with idarubicin and etoposide on RFS, EFS and OS
- To evaluate the impact of 5-azacytidine maintenance therapy in patients achieving a CR on RFS and OS
- To evaluate the efficacy of lenograstim based on duration of neutro- and leukopenia as well as incidence of infection and duration of hospitalization after consolidation therapy
- Assessment of quality of life

Safety Objectives
- Evaluation of safety based on toxicity induced by 5-azacytidine

Protection of trial subjects:

In this study, safety was assessed by evaluating the following: reported adverse events, clinical laboratory test results, vital signs measurements, ECG findings, chest X-ray, echo scan, physical examination findings, monitoring of concomitant therapy. For each safety parameter, all findings (whether normal or abnormal) were recorded in the CRF.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 21
Country: Number of subjects enrolled	Germany: 256
Worldwide total number of subjects	277
EEA total number of subjects	277

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	161
From 65 to 84 years	116
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First Patient in: 22.10.2010
Last Patient in: 03.04.2012
Recruitment was not interrupted, but randomization into Treatment arms B and C was stopped with effective date 16 September 2011 due to unsufficient efficacy.

Pre-assignment

Screening details:

Molecular genetic analysis (central AMLSG reference lab) of blood and bone marrow was performed at baseline within 48 hours to make an enrollment possible.

Pre-assignment period milestones

Number of subjects started	277
Number of subjects completed	268

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Violation of inclusion/exclusion criteria: 6
Reason: Number of subjects	Consent withdrawn by subject: 2
Reason: Number of subjects	Other: 1

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Standard

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy: 100 mg/m2/day by continuous IV infusion on days 1-7 (total dose 700 mg/m2)
Consolidation therapy: Younger adults (18 to 65 yrs): 3 g/m2/day by IV infusion over 3 hours every 12 hours on days 1, 2, and 3 (total dose 18 g/m2).
Elderly patients (>65 yrs): 1 g/m2/day by IV infusion over 3 hours every 12 hours on days 1, 2, and 3 (total dose 6 g/m2).

Investigational medicinal product name	Idarubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy cycle 1: 12 mg/m2/day by IV push on days 1,3,5 (total dose 36 mg/m2). For elderly

(>65 yrs) patients only two doses of idarubicin were foreseen on days 1+3.
Induction therapy cycle 2: 12 mg/m2/day by IV push on days 1 and 3 (total dose 24 mg/m2; for all age groups).

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy: 100 mg/m²/day by 1-hour IV infusion on days 1,2,3 (total dose 300 mg/m2). On days 1 and 3 start after idarubicin push. For elderly (>65 yrs) patients only two doses of etoposide were foreseen on days 1+3.

Arm title	Arm B: Aza prior

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder, dispersion and solvent for concentrate for dispersion for infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Induction therapy: 100 mg/m2/day by SC injection or 15-minute IV infusion on day 1 to day 5 (total dose 500 mg/m2). Azacitidine was given prior to idarubicin and etoposide.

Investigational medicinal product name	Idarubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy cycle 1: 12 mg/m2/day by IV push on days 6, 8 10 (total dose 36 mg/m2). For elderly (>65 yrs) patients only two doses of idarubicin were foreseen on days 6+8.
Induction therapy cycle 2: 12 mg/m2/day by IV push on days 6 and 8 (total dose 24 mg/m2; for all age groups).

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy: 100 mg/m²/day by 1-hour IV infusion on days 6,7,8 (total dose 300 mg/m2). On days 1 and 3 start after idarubicin push. For elderly (>65 yrs) patients only two doses of etoposide were foreseen on days 6+8.

Arm title	Arm C: Aza concurrent

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder, dispersion and solvent for concentrate for dispersion for infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Induction therapy:100 mg/m2/day by SC injection or 15-minute IV infusion on days 1-5 (total dose 500 mg/m2). Azacitidine was given prior to idarubicin and etoposide..

Investigational medicinal product name	Idarubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy cycle 1: 12 mg/m2/day by IV push on days 1,3,5 (total dose 36 mg/m2). For elderly (>65 yrs) patients only two doses of idarubicin were foreseen on days 1+3.
Induction therapy cycle 2: 12 mg/m2/day by IV push on days 1 and 3 (total dose 24 mg/m2; for all age groups).

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy: 100 mg/m²/day by 1-hour IV infusion on days 1,2,3 (total dose 300 mg/m2). On days 1 and 3 start after idarubicin push. For elderly (>65 yrs) patients only two doses of etoposide were foreseen on days 1+3.

Arm title	Arm D: Aza after

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder, dispersion and solvent for concentrate for dispersion for infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Induction therapy:100 mg/m2/day by SC injection or 15-minute IV infusion on days 4-8 (total dose 500 mg/m2). Azacitidine was given prior to idarubicin and etoposide.

Investigational medicinal product name	Idarubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy cycle 1: 12 mg/m2/day by IV push on days 1,3,5 (total dose 36 mg/m2). For elderly (>65 yrs) patients only two doses of idarubicin were foreseen on days 1+3.
Induction therapy cycle 2: 12 mg/m2/day by IV push on days 1 and 3 (total dose 24 mg/m2; for all age groups).

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction therapy: 100 mg/m²/day by 1-hour IV infusion on days 1,2,3 (total dose 300 mg/m2). On days 1 and 3 start after idarubicin push. For elderly (>65 yrs) patients only two doses of etoposide were foreseen on days 1+3.

Number of subjects in period 1[1]	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent
Started	100	35	34
Completed	39	6	5
Not completed	61	29	29
Adverse event, serious fatal	4	3	2
Consent withdrawn by subject	2	-	1
Adverse event, non-fatal	11	4	1
Other	4	-	1
Lack of efficacy	40	22	24

Number of subjects in period 1[1]	Arm D: Aza after
Started	99
Completed	22
Not completed	77
Adverse event, serious fatal	8
Consent withdrawn by subject	2
Adverse event, non-fatal	7
Other	3
Lack of efficacy	57

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the 277 patients who were enrolled to the study 9 patients were excluded due to violation of inclusion/exclusion criteria (n=6: no presence of AML n=3, AML with NPM1 mutation n=1, presence of Philadelphia chromosome n=1, organ insufficiency (renal failure) n=1), withdrawal of informed consent (n=2) and other reason (extramedullary manifestation of AML in spleen, n=1).

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: Standard
Reporting group description: -	
Reporting group title	Arm B: Aza prior
Reporting group description: -	
Reporting group title	Arm C: Aza concurrent
Reporting group description: -	
Reporting group title	Arm D: Aza after
Reporting group description: -	

Reporting group values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent
Number of subjects	100	35	34
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	62.6	63.5	63.6
full range (min-max)	19 to 81	20 to 79	36 to 82
Gender categorical Units: Subjects			
Female	51	14	20
Male	49	21	14
ECOG Performance Status Units: Subjects			
ECOG 0	42	16	13
ECOG 1	53	16	20
ECOG 2	5	3	1
Type of AML Units: Subjects			
De Novo AML	73	24	24
sAML	16	8	8
tAML	11	3	2
CEBPA mutation status Units: Subjects			
Wildtype	82	28	29
Single mutation	4	0	0

Double mutation	7	1	1
Not recorded	7	6	4
DNMT3A mutation status Units: Subjects			
Wildtype	76	23	24
Mutation	17	6	6
Not recorded	7	6	4
ASXL1 mutation status Units: Subjects			
Wildtype	66	22	26
Mutation	16	5	2
Not recorded	18	8	6
RUNX1 mutation status Units: Subjects			
Wildtype	78	19	21
Mutation	15	8	9
not recorded	7	8	4
IDH1 mutation status Units: Subjects			
Wildtype	79	24	26
Mutation	13	3	3
not recorded	8	8	5
IDH2 mutation status Units: Subjects			
Wildtype	77	25	23
Mutation	5	3	6
not recorded	18	7	5
ELN 2010 classification Units: Subjects			
Favorable	7	1	0
Intermediate-I	31	9	11
Intermediate-II	16	12	9
Adverse	30	11	5
not applicable	16	2	9
Hemoglobin (g/dl) Units: g/dl			
median	9.1	9.8	9.6
full range (min-max)	5.2 to 12.9	5.9 to 12.9	6.9 to 13.6
Platelets (G/l) Units: G/l			
median	64.5	61	53
full range (min-max)	3 to 419	16 to 1286	12 to 301
White blood count (G/l) Units: G/l			
median	3.0	3.4	3.6
full range (min-max)	0.4 to 186.0	0.8 to 155.2	0.6 to 141.3
Bone marrow blasts (%) Units: percent			
median	53	63.5	61.5
full range (min-max)	0 to 100	10 to 100	20 to 93
Peripheral blood blasts (%)			

Units: percent			
median	12	16	5
full range (min-max)	0 to 97	0 to 88	0 to 92

Reporting group values	Arm D: Aza after	Total	
Number of subjects	99	268	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	62.3		
full range (min-max)	18 to 79	-	
Gender categorical			
Units: Subjects			
Female	39	124	
Male	60	144	
ECOG Performance Status			
Units: Subjects			
ECOG 0	42	113	
ECOG 1	47	136	
ECOG 2	10	19	
Type of AML			
Units: Subjects			
De Novo AML	76	197	
sAML	18	50	
tAML	5	21	
CEBPA mutation status			
Units: Subjects			
Wildtype	76	215	
Single mutation	2	6	
Double mutation	8	17	
Not recorded	13	30	
DNMT3A mutation status			
Units: Subjects			
Wildtype	72	195	
Mutation	11	40	
Not recorded	16	33	
ASXL1 mutation status			
Units: Subjects			
Wildtype	67	181	
Mutation	9	32	

Not recorded	23	55	
RUNX1 mutation status Units: Subjects			
Wildtype	69	187	
Mutation	14	46	
not recorded	16	35	
IDH1 mutation status Units: Subjects			
Wildtype	77	206	
Mutation	6	25	
not recorded	16	37	
IDH2 mutation status Units: Subjects			
Wildtype	63	188	
Mutation	13	27	
not recorded	23	53	
ELN 2010 classification Units: Subjects			
Favorable	6	14	
Intermediate-I	28	79	
Intermediate-II	23	60	
Adverse	31	77	
not applicable	11	38	
Hemoglobin (g/dl) Units: g/dl			
median	9.1		
full range (min-max)	5.6 to 13.8	-	
Platelets (G/l) Units: G/l			
median	67		
full range (min-max)	4 to 956	-	
White blood count (G/l) Units: G/l			
median	4.2		
full range (min-max)	0.3 to 214.0	-	
Bone marrow blasts (%) Units: percent			
median	60		
full range (min-max)	0 to 99	-	
Peripheral blood blasts (%) Units: percent			
median	8.5		
full range (min-max)	0 to 97	-	

Subject analysis sets

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set contained all patients scheduled for study treatment.

Subject analysis set title	Primary endpoint analysis set

Subject analysis set type	Intention-to-treat

Subject analysis set description:

Data of all patients scheduled for study treatment (n=268) were considered for efficacy and safety analyses. According to statistical analysis planning, 220 eligible patients were included into analysis of primary endpoint (= primary endpoint analysis set).

Reporting group values	Full analysis set	Primary endpoint analysis set	
Number of subjects	268	220	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	62.6		
full range (min-max)	18 to 82		
Gender categorical Units: Subjects			
Female	124		
Male	144		
ECOG Performance Status Units: Subjects			
ECOG 0	113		
ECOG 1	136		
ECOG 2	19		
Type of AML Units: Subjects			
De Novo AML	197		
sAML	50		
tAML	21		
CEBPA mutation status Units: Subjects			
Wildtype	215		
Single mutation	6		
Double mutation	17		
Not recorded	30		
DNMT3A mutation status Units: Subjects			
Wildtype	195		
Mutation	40		
Not recorded	33		
ASXL1 mutation status Units: Subjects			

Wildtype	181		
Mutation	32		
Not recorded	55		
RUNX1 mutation status Units: Subjects			
Wildtype	187		
Mutation	46		
not recorded	35		
IDH1 mutation status Units: Subjects			
Wildtype	206		
Mutation	25		
not recorded	37		
IDH2 mutation status Units: Subjects			
Wildtype	188		
Mutation	27		
not recorded	53		
ELN 2010 classification Units: Subjects			
Favorable	14		
Intermediate-I	79		
Intermediate-II	60		
Adverse	77		
not applicable	38		
Hemoglobin (g/dl) Units: g/dl			
median	9.2		
full range (min-max)	5.2 to 13.8		
Platelets (G/l) Units: G/l			
median	63.5		
full range (min-max)	3 to 1286		
White blood count (G/l) Units: G/l			
median	3.7		
full range (min-max)	0.3 to 214.0		
Bone marrow blasts (%) Units: percent			
median	60		
full range (min-max)	0 to 100		
Peripheral blood blasts (%) Units: percent			
median	10		
full range (min-max)	0 to 97		

End points

End points reporting groups

Reporting group title	Arm A: Standard
Reporting group description: -	
Reporting group title	Arm B: Aza prior
Reporting group description: -	
Reporting group title	Arm C: Aza concurrent
Reporting group description: -	
Reporting group title	Arm D: Aza after
Reporting group description: -	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set contained all patients scheduled for study treatment.	
Subject analysis set title	Primary endpoint analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Data of all patients scheduled for study treatment (n=268) were considered for efficacy and safety analyses. According to statistical analysis planning, 220 eligible patients were included into analysis of primary endpoint (= primary endpoint analysis set).	

Primary: CR rate after induction therapy (primary endpoint analysis set)

End point title	CR rate after induction therapy (primary endpoint analysis
End point description:	
The null hypothesis in each arm was H0: π ≤ 0.40, whereby π denoted the true CR rate of the induction therapy. In contrast, an effective therapy should achieve at least a CR rate of 55%. The sample size was calculated to detect an effective therapy with a power of 80%. The level of significance was fixed at α=5% for each treatment arm. Based on the „optimal two-stage design" of Simon, an efficacy of the corresponding therapy would be rejected in the first stage of 26 treated patients, if 11 or less patients achieved a CR (or CRi). If 12 or more patients achieved a CR (or CRi) during this first stage, the trial would be continued to second stage with a total sample size of 84 patients per treatment arm. If more than 40 of 84 evaluable patients achieved a CR (or CRi), the null hypothesis of the corresponding treatment arm could be rejected and the treatment arm could be judged as effective therapy.	
End point type	Primary
End point timeframe:	
after induction therapy (two months)	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Primary endpoint was analyzed according to Simon's two stage design. An effective therapy should have achieved a CR in more than 40 of 84 patients. The null hypothesis for treatment arm D could not be rejected, since there were only 37 patients who achieved a CR/CRi. Since 45 patients achieved a CR/CRi in arm A, the standard arm was judged as the sole effective treatment arm of the study with an estimated CR rate of 55.5% and a lower limit of a one-sided 95% confidence interval of 46.3%.	

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	26	26	84
Units: Subjects with Complete remission	45	11	10	37

End point values	Primary endpoint analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	220			
Units: Subjects with Complete remission	103			

Statistical analyses

No statistical analyses for this end point

Secondary: CR rate after induction therapy (full data set)

End point title	CR rate after induction therapy (full data set)

End point description:

End point type	Secondary

End point timeframe:

CR rate after induction therapy (two months)

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	35	34	99
Units: Subjects with complete remission	54	14	12	46

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	268			
Units: Subjects with complete remission	126			

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival after four years

End point title	Event-free Survival after four years

End point description:

As events the following were considered according to study protocol: death during induction therapy,

refractory disease after first induction therapy, refractory disease or partial response after second induction therapy, relapse and death in CR. Time between study entry and occurrence of the first event was analyzed.

End point type	Secondary
End point timeframe: after four years	

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	35	34	99
Units: Percentage				
number (confidence interval 95%)	23.8 (16.6 to 34.2)	8.6 (2.9 to 25.3)	19.0 (9.3 to 38.7)	10.1 (5.6 to 18.2)

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	268			
Units: Percentage				
number (confidence interval 95%)	16.1 (12.2 to 21.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-free Survival after four years

End point title	Relapse-free Survival after four years
End point description:	
End point type	Secondary
End point timeframe: after four years	

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	14	12	46
Units: Percentage				
number (confidence interval 95%)	36.0 (25.1 to 51.7)	21.4 (7.9 to 58.4)	41.7 (21.3 to 81.4)	21.7 (12.6 to 37.6)

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	126			
Units: Percentage				
number (confidence interval 95%)	29.8 (22.8 to 39.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative incidence of relapse

End point title	Cumulative incidence of relapse

End point description:

End point type	Secondary

End point timeframe:

after four years

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	14	12	46
Units: Percentage				
number (not applicable)	50.9	57.1	50.0	60.9

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	126			
Units: Percentage				
number (not applicable)	55.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative incidence of death

End point title	Cumulative incidence of death

End point description:

End point type	Secondary

End point timeframe:
after four years

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	14	12	46
Units: Percentage				
number (not applicable)	13.1	21.4	8.3	17.4

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	126			
Units: Percentage				
number (not applicable)	15.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival after four years

End point title	Overall survival after four years

End point description:

End point type	Secondary

End point timeframe:
after four years

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	35	34	99
Units: Percentage				
number (confidence interval 95%)	36.6 (28.1 to 47.6)	20.0 (10.3 to 38.8)	29.4 (17.5 to 49.5)	25.5 (4.5 to 38.1)

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	268			
Units: Percentage				
number (confidence interval 95%)	29.4 (24.3 to 35.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Nights in hospital (overall trial)

End point title	Nights in hospital (overall trial)

End point description:

End point type	Secondary

End point timeframe:

Whole Trial (max. 30 months)

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	35	34	99
Units: Nights				
median (full range (min-max))	65 (16 to 171)	40 (14 to 150)	43.5 (18 to 156)	58 (3 to 172)

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	268			
Units: Nights				
median (full range (min-max))	55 (3 to 172)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of Leukopenia after consolidation therapy

End point title	Median duration of Leukopenia after consolidation therapy

End point description:

End point type	Secondary

End point timeframe:
within the first six months of therapy

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	4	7	24
Units: Days				
number (not applicable)				
Consolidation cycle 1	16	16	14	15.5
Consolidation cycle 2	17	15	15	15
Consolidation cycle 3	17.5	15	22.5	15

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of neutropenia after consolidation therapy

End point title	Median duration of neutropenia after consolidation therapy

End point description:

End point type	Secondary

End point timeframe:
within the first six months of therapy

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	3	7	22
Units: Days				
number (not applicable)				
Consolidation cycle 1	18	16	24	18
Consolidation cycle 2	18	16	16	15
Consolidation cycle 3	19.5	17	27	17

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of thrombocytopenia after consolidation therapy

End point title	Median duration of thrombocytopenia after consolidation therapy

End point description:

End point type	Secondary

End point timeframe:
within the first six months of therapy

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	4	7	24
Units: Days				
number (not applicable)				
Consolidation cycle 1	22	20	17	16
Consolidation cycle 2	28	18	19	18
Consolidation cycle 3	20	17	23.5	16.5

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Health (Global health status)

End point title	Quality of Health (Global health status)

End point description:

End point type	Secondary

End point timeframe:
at baseline and at the end of Treatment (maximal after 30 months)

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	4	7	37
Units: Score value %				
median (full range (min-max))				
Baseline	50 (16.7 to 83.3)	54.2 (16.7 to 100)	33.3 (16.7 to 100)	50 (0 to 100)
End of treatment	75 (16.7 to 100)	41.7 (16.7 to 50)	41.7 (41.7 to 41.7)	58.3 (33.3 to 83.3)

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	81			
Units: Score value %				
median (full range (min-max))				
Baseline End of treatment	50 (0 to 100) 66.7 (16.7 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Early / Hypoplastic Death (ED/HD)

End point title	Rate of Early / Hypoplastic Death (ED/HD)

End point description:

End point type	Secondary

End point timeframe:

within the first two months of therapy (induction therapy)

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	35	34	99
Units: Rate				
number (confidence interval 95%)	2.0 (0.6 to 7.0)	5.7 (1.6 to 18.6)	5.9 (1.6 to 19.0)	6.0 (2.8 to 12.6)

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	268			
Units: Rate				
number (confidence interval 95%)	4.5 (2.6 to 7.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of leukopenia after induction therapy

End point title	Median duration of leukopenia after induction therapy

End point description:

End point type	Secondary

End point timeframe:
within the first two months (induction therapy)

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	34	34	98
Units: Days				
number (not applicable)				
Induction cycle 1	24	27	25	27
Induction cycle 2	26	26	25	25

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of neutropenia after induction therapy

End point title	Median duration of neutropenia after induction therapy

End point description:

End point type	Secondary

End point timeframe:
within the first two months (induction therapy)

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	82	28	29	81
Units: Days				
number (not applicable)				
Induction cycle 1	31	30	40	33
Induction cycle 2	36	31	35	35

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of thrombocytopenia after induction therapy

End point title	Median duration of thrombocytopenia after induction therapy

End point description:

End point type	Secondary

End point timeframe:

within the first two months (induction therapy)

End point values	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent	Arm D: Aza after
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	34	34	98
Units: Days				
number (not applicable)				
Induction cycle 1	25	29	28	22
Induction cycle 2	26	23	25	19

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event reporting period for this trial began upon signing of informed consent and ended 28 days after the last treatment Administration.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	Arm A: Standard
Reporting group description: -	
Reporting group title	Arm B: Aza prior
Reporting group description: -	
Reporting group title	Arm C: Aza concurrent
Reporting group description: -	
Reporting group title	Arm D: Aza after

Reporting group description: -

Serious adverse events	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 100 (30.00%)	11 / 35 (31.43%)	12 / 34 (35.29%)
number of deaths (all causes)	4	3	2
number of deaths resulting from adverse events	4	3	2
Vascular disorders			
CNS Hemorrhage			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemorrhage pulmonary			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemorrhage, GU			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis/embolism			

subjects affected / exposed	0 / 100 (0.00%)	1 / 35 (2.86%)	0 / 34 (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
General disorders and administration site conditions			
Constitutional symptoms - other			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (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
Death not associated with CTCAE			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Allergy - Other			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (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
Leukocytes			
subjects affected / exposed	2 / 100 (2.00%)	1 / 35 (2.86%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ARDS			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnea			

subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 100 (0.00%)	1 / 35 (2.86%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular arrhythmia			
subjects affected / exposed	2 / 100 (2.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac general - other			
subjects affected / exposed	2 / 100 (2.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac ischemia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary arrest			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (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 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Confusion			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (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
Seizure			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Blood - Other			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow cellularity			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemoglobin			

subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophils			
subjects affected / exposed	1 / 100 (1.00%)	1 / 35 (2.86%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelets			
subjects affected / exposed	2 / 100 (2.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic function			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (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
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	2 / 100 (2.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhea			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucositis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain - Gastrointestinal: Abdomen NOS			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (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 - other			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver dysfunction			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatology - Other			
subjects affected / exposed	0 / 100 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rash			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal - other			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal - other: Fluid retention/edema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Diabetes			
subjects affected / exposed	0 / 100 (0.00%)	1 / 35 (2.86%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal - other			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain - Musculoskeletal: joint			

subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Febrile neutropenia			
subjects affected / exposed	3 / 100 (3.00%)	2 / 35 (5.71%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	2 / 3	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection - Catheter-related			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection - Gastrointestinal Abdomen NOS			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection - Gastrointestinal anal/perianal			
subjects affected / exposed	0 / 100 (0.00%)	2 / 35 (5.71%)	0 / 34 (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
Infection - Gastrointestinal - Appendix			
subjects affected / exposed	2 / 100 (2.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection - other			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (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
Sepsis			
subjects affected / exposed	5 / 100 (5.00%)	3 / 35 (8.57%)	5 / 34 (14.71%)
occurrences causally related to treatment / all	4 / 5	0 / 3	3 / 5
deaths causally related to treatment / all	1 / 2	0 / 2	1 / 2

Infection with grade 3/4 neutrophils			
subjects affected / exposed	1 / 100 (1.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection - Soft tissue NOS			
subjects affected / exposed	0 / 100 (0.00%)	2 / 35 (5.71%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung (Pneumonia)			
subjects affected / exposed	5 / 100 (5.00%)	1 / 35 (2.86%)	3 / 34 (8.82%)
occurrences causally related to treatment / all	4 / 5	1 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Metabolism and nutrition disorders			
Hypokalemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 35 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm D: Aza after		
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 99 (32.32%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	8		
Vascular disorders			
CNS Hemorrhage			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hemorrhage pulmonary			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hemorrhage, GU			

subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis/embolism			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Constitutional symptoms - other			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death not associated with CTCAE			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Immune system disorders			
Allergic reaction			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Allergy - Other			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukocytes			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ARDS			

subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Dyspnea				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 99 (2.02%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Supraventricular arrhythmia				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular arrhythmia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac general - other				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac ischemia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiopulmonary arrest				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Restrictive cardiomyopathy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Confusion				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Blood - Other				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bone marrow cellularity				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemoglobin				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutrophils				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Platelets				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic function				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Retinal detachment				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Colitis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Diarrhea				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				

subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mucositis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain - Gastrointestinal: Abdomen NOS				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary - other				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Liver dysfunction				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				

Dermatology - Other			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal - other			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal - other: Fluid retention/edema			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Diabetes			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal - other			

subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pain - Musculoskeletal: joint				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Febrile neutropenia				
subjects affected / exposed	3 / 99 (3.03%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Infection - Catheter-related				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection - Gastrointestinal Abdomen NOS				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection - Gastrointestinal anal/perianal				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection - Gastrointestinal - Appendix				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection - other				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Sepsis			
subjects affected / exposed	9 / 99 (9.09%)		
occurrences causally related to treatment / all	5 / 9		
deaths causally related to treatment / all	2 / 3		
Infection with grade 3/4 neutrophils			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection - Soft tissue NOS			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung (Pneumonia)			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalemia			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Arm A: Standard	Arm B: Aza prior	Arm C: Aza concurrent
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 100 (100.00%)	35 / 35 (100.00%)	34 / 34 (100.00%)
Vascular disorders			
Hematoma			
subjects affected / exposed	15 / 100 (15.00%)	2 / 35 (5.71%)	4 / 34 (11.76%)
occurrences (all)	27	2	5
Hemorrhage pulmonary			
subjects affected / exposed	22 / 100 (22.00%)	3 / 35 (8.57%)	7 / 34 (20.59%)
occurrences (all)	31	3	10

Hemorrhage, GI			
subjects affected / exposed	5 / 100 (5.00%)	3 / 35 (8.57%)	2 / 34 (5.88%)
occurrences (all)	7	4	2
Petechiae			
subjects affected / exposed	17 / 100 (17.00%)	7 / 35 (20.00%)	7 / 34 (20.59%)
occurrences (all)	30	9	10
Phlebitis			
subjects affected / exposed	6 / 100 (6.00%)	7 / 35 (20.00%)	2 / 34 (5.88%)
occurrences (all)	7	10	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 100 (22.00%)	7 / 35 (20.00%)	6 / 34 (17.65%)
occurrences (all)	39	9	9
Fever neonatal			
subjects affected / exposed	38 / 100 (38.00%)	8 / 35 (22.86%)	11 / 34 (32.35%)
occurrences (all)	87	23	13
Insomnia			
subjects affected / exposed	35 / 100 (35.00%)	6 / 35 (17.14%)	9 / 34 (26.47%)
occurrences (all)	84	12	15
Rigors/chills			
subjects affected / exposed	8 / 100 (8.00%)	0 / 35 (0.00%)	5 / 34 (14.71%)
occurrences (all)	10	0	5
Weight gain			
subjects affected / exposed	22 / 100 (22.00%)	4 / 35 (11.43%)	3 / 34 (8.82%)
occurrences (all)	36	6	6
Pain NOS			
subjects affected / exposed	18 / 100 (18.00%)	5 / 35 (14.29%)	8 / 34 (23.53%)
occurrences (all)	23	5	16
Pain - other			
subjects affected / exposed	8 / 100 (8.00%)	3 / 35 (8.57%)	4 / 34 (11.76%)
occurrences (all)	10	3	5
Immune system disorders			
Allergic reaction			
subjects affected / exposed	19 / 100 (19.00%)	5 / 35 (14.29%)	4 / 34 (11.76%)
occurrences (all)	23	7	10
Respiratory, thoracic and mediastinal disorders			

Pain chest/thorax			
subjects affected / exposed	6 / 100 (6.00%)	4 / 35 (11.43%)	2 / 34 (5.88%)
occurrences (all)	7	4	3
Pain throat/pharynx			
subjects affected / exposed	8 / 100 (8.00%)	1 / 35 (2.86%)	1 / 34 (2.94%)
occurrences (all)	9	1	1
Cough			
subjects affected / exposed	12 / 100 (12.00%)	4 / 35 (11.43%)	5 / 34 (14.71%)
occurrences (all)	15	6	5
Dyspnea			
subjects affected / exposed	11 / 100 (11.00%)	4 / 35 (11.43%)	5 / 34 (14.71%)
occurrences (all)	18	5	8
Investigations			
Coagulation - other			
subjects affected / exposed	10 / 100 (10.00%)	3 / 35 (8.57%)	3 / 34 (8.82%)
occurrences (all)	13	3	5
ALT			
subjects affected / exposed	7 / 100 (7.00%)	2 / 35 (5.71%)	3 / 34 (8.82%)
occurrences (all)	14	2	5
AST			
subjects affected / exposed	7 / 100 (7.00%)	2 / 35 (5.71%)	2 / 34 (5.88%)
occurrences (all)	10	3	5
Bilirubin			
subjects affected / exposed	14 / 100 (14.00%)	1 / 35 (2.86%)	2 / 34 (5.88%)
occurrences (all)	19	1	2
Creatinine			
subjects affected / exposed	7 / 100 (7.00%)	2 / 35 (5.71%)	3 / 34 (8.82%)
occurrences (all)	9	3	5
Hyperglycemia			
subjects affected / exposed	5 / 100 (5.00%)	1 / 35 (2.86%)	1 / 34 (2.94%)
occurrences (all)	6	1	1
Hyperuricemia			
subjects affected / exposed	6 / 100 (6.00%)	2 / 35 (5.71%)	4 / 34 (11.76%)
occurrences (all)	8	3	4
Hypocalcemia			

subjects affected / exposed	9 / 100 (9.00%)	1 / 35 (2.86%)	1 / 34 (2.94%)
occurrences (all)	14	3	1
Hypokalemia			
subjects affected / exposed	57 / 100 (57.00%)	8 / 35 (22.86%)	12 / 34 (35.29%)
occurrences (all)	115	20	22
Hypomagnesemia			
subjects affected / exposed	9 / 100 (9.00%)	2 / 35 (5.71%)	2 / 34 (5.88%)
occurrences (all)	14	2	2
Hyponatremia			
subjects affected / exposed	5 / 100 (5.00%)	0 / 35 (0.00%)	4 / 34 (11.76%)
occurrences (all)	6	0	4
Investigations: other			
subjects affected / exposed	14 / 100 (14.00%)	2 / 35 (5.71%)	3 / 34 (8.82%)
occurrences (all)	36	7	4
CRP increase			
subjects affected / exposed	15 / 100 (15.00%)	3 / 35 (8.57%)	5 / 34 (14.71%)
occurrences (all)	25	10	9
Cardiac disorders			
Supraventricular arrhythmia			
subjects affected / exposed	8 / 100 (8.00%)	3 / 35 (8.57%)	7 / 34 (20.59%)
occurrences (all)	11	3	9
Hypertension			
subjects affected / exposed	24 / 100 (24.00%)	9 / 35 (25.71%)	6 / 34 (17.65%)
occurrences (all)	33	10	18
Hypotension			
subjects affected / exposed	9 / 100 (9.00%)	1 / 35 (2.86%)	2 / 34 (5.88%)
occurrences (all)	11	1	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	18 / 100 (18.00%)	7 / 35 (20.00%)	6 / 34 (17.65%)
occurrences (all)	28	7	6
Agitation			
subjects affected / exposed	5 / 100 (5.00%)	3 / 35 (8.57%)	3 / 34 (8.82%)
occurrences (all)	6	3	3
Anxiety			

subjects affected / exposed	11 / 100 (11.00%)	4 / 35 (11.43%)	5 / 34 (14.71%)
occurrences (all)	19	5	5
Depression			
subjects affected / exposed	7 / 100 (7.00%)	5 / 35 (14.29%)	6 / 34 (17.65%)
occurrences (all)	11	8	7
Head/Headache			
subjects affected / exposed	25 / 100 (25.00%)	9 / 35 (25.71%)	5 / 34 (14.71%)
occurrences (all)	44	17	7
Blood and lymphatic system disorders			
Hemoglobin			
subjects affected / exposed	95 / 100 (95.00%)	28 / 35 (80.00%)	28 / 34 (82.35%)
occurrences (all)	247	53	63
Leukocytes			
subjects affected / exposed	72 / 100 (72.00%)	24 / 35 (68.57%)	25 / 34 (73.53%)
occurrences (all)	180	48	62
Neutrophils			
subjects affected / exposed	38 / 100 (38.00%)	15 / 35 (42.86%)	14 / 34 (41.18%)
occurrences (all)	94	28	31
Platelets			
subjects affected / exposed	95 / 100 (95.00%)	29 / 35 (82.86%)	28 / 34 (82.35%)
occurrences (all)	256	55	73
Gastrointestinal disorders			
Anorexia			
subjects affected / exposed	16 / 100 (16.00%)	5 / 35 (14.29%)	4 / 34 (11.76%)
occurrences (all)	20	5	7
Constipation			
subjects affected / exposed	38 / 100 (38.00%)	12 / 35 (34.29%)	10 / 34 (29.41%)
occurrences (all)	61	16	19
Diarrhea			
subjects affected / exposed	51 / 100 (51.00%)	13 / 35 (37.14%)	11 / 34 (32.35%)
occurrences (all)	89	20	17
Heartburn			
subjects affected / exposed	6 / 100 (6.00%)	1 / 35 (2.86%)	4 / 34 (11.76%)
occurrences (all)	12	2	6
Mucositis			

subjects affected / exposed	39 / 100 (39.00%)	8 / 35 (22.86%)	13 / 34 (38.24%)
occurrences (all)	56	10	16
Nausea			
subjects affected / exposed	61 / 100 (61.00%)	18 / 35 (51.43%)	23 / 34 (67.65%)
occurrences (all)	128	33	51
Vomiting			
subjects affected / exposed	28 / 100 (28.00%)	10 / 35 (28.57%)	15 / 34 (44.12%)
occurrences (all)	40	12	22
Pain Abdomen NOS			
subjects affected / exposed	22 / 100 (22.00%)	6 / 35 (17.14%)	5 / 34 (14.71%)
occurrences (all)	32	7	5
Pain Stomach			
subjects affected / exposed	10 / 100 (10.00%)	8 / 35 (22.86%)	4 / 34 (11.76%)
occurrences (all)	14	9	5
Skin and subcutaneous tissue disorders			
Dermatology - other			
subjects affected / exposed	11 / 100 (11.00%)	4 / 35 (11.43%)	2 / 34 (5.88%)
occurrences (all)	15	8	6
Injection site reaction			
subjects affected / exposed	15 / 100 (15.00%)	8 / 35 (22.86%)	9 / 34 (26.47%)
occurrences (all)	23	12	24
Pruritus			
subjects affected / exposed	11 / 100 (11.00%)	2 / 35 (5.71%)	2 / 34 (5.88%)
occurrences (all)	17	3	2
Rash			
subjects affected / exposed	31 / 100 (31.00%)	9 / 35 (25.71%)	11 / 34 (32.35%)
occurrences (all)	57	16	16
Renal and urinary disorders			
Fluid retention/edema			
subjects affected / exposed	53 / 100 (53.00%)	12 / 35 (34.29%)	17 / 34 (50.00%)
occurrences (all)	89	30	32
Musculoskeletal and connective tissue disorders			
Musculoskeletal - other			
subjects affected / exposed	5 / 100 (5.00%)	3 / 35 (8.57%)	1 / 34 (2.94%)
occurrences (all)	6	3	1
Pain back			

subjects affected / exposed	17 / 100 (17.00%)	3 / 35 (8.57%)	3 / 34 (8.82%)
occurrences (all)	23	3	4
Pain bone			
subjects affected / exposed	7 / 100 (7.00%)	2 / 35 (5.71%)	1 / 34 (2.94%)
occurrences (all)	9	2	1
Pain Extremity/Limb			
subjects affected / exposed	6 / 100 (6.00%)	2 / 35 (5.71%)	2 / 34 (5.88%)
occurrences (all)	8	2	2
Pain: Joint			
subjects affected / exposed	4 / 100 (4.00%)	4 / 35 (11.43%)	1 / 34 (2.94%)
occurrences (all)	7	4	1
Infections and infestations			
Infection: Lip/perioral			
subjects affected / exposed	9 / 100 (9.00%)	4 / 35 (11.43%)	1 / 34 (2.94%)
occurrences (all)	12	4	1
Febrile neutropenia			
subjects affected / exposed	52 / 100 (52.00%)	18 / 35 (51.43%)	16 / 34 (47.06%)
occurrences (all)	91	24	27
Infection: Catheter-related			
subjects affected / exposed	12 / 100 (12.00%)	9 / 35 (25.71%)	3 / 34 (8.82%)
occurrences (all)	17	10	5
Infection - other			
subjects affected / exposed	32 / 100 (32.00%)	5 / 35 (14.29%)	6 / 34 (17.65%)
occurrences (all)	58	8	7
Sepsis			
subjects affected / exposed	23 / 100 (23.00%)	5 / 35 (14.29%)	8 / 34 (23.53%)
occurrences (all)	36	9	14
Infection with grade 3/4 neutrophils			
subjects affected / exposed	8 / 100 (8.00%)	1 / 35 (2.86%)	1 / 34 (2.94%)
occurrences (all)	13	1	1
Infection with unknown ANC			
subjects affected / exposed	5 / 100 (5.00%)	2 / 35 (5.71%)	1 / 34 (2.94%)
occurrences (all)	11	2	3
Lung (pneumonia)			
subjects affected / exposed	23 / 100 (23.00%)	9 / 35 (25.71%)	4 / 34 (11.76%)
occurrences (all)	35	11	9

Infection: Urinary tract NOS			
subjects affected / exposed	7 / 100 (7.00%)	1 / 35 (2.86%)	3 / 34 (8.82%)
occurrences (all)	11	1	3

Non-serious adverse events	Arm D: Aza after		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 99 (100.00%)		
Vascular disorders			
Hematoma			
subjects affected / exposed	9 / 99 (9.09%)		
occurrences (all)	9		
Hemorrhage pulmonary			
subjects affected / exposed	20 / 99 (20.20%)		
occurrences (all)	27		
Hemorrhage, GI			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	9		
Petechiae			
subjects affected / exposed	19 / 99 (19.19%)		
occurrences (all)	21		
Phlebitis			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	10		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 99 (19.19%)		
occurrences (all)	26		
Fever neonatal			
subjects affected / exposed	33 / 99 (33.33%)		
occurrences (all)	53		
Insomnia			
subjects affected / exposed	38 / 99 (38.38%)		
occurrences (all)	52		
Rigors/chills			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Weight gain			

subjects affected / exposed	13 / 99 (13.13%)		
occurrences (all)	19		
Pain NOS			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	8		
Pain - other			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	7		
Immune system disorders			
Allergic reaction			
subjects affected / exposed	19 / 99 (19.19%)		
occurrences (all)	28		
Respiratory, thoracic and mediastinal disorders			
Pain chest/thorax			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Pain throat/pharynx			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	9		
Cough			
subjects affected / exposed	25 / 99 (25.25%)		
occurrences (all)	29		
Dyspnea			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	15		
Investigations			
Coagulation - other			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	7		
ALT			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
AST			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Bilirubin			

subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	6		
Creatinine			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	12		
Hyperglycemia			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	11		
Hyperuricemia			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	4		
Hypocalcemia			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	11		
Hypokalemia			
subjects affected / exposed	38 / 99 (38.38%)		
occurrences (all)	67		
Hypomagnesemia			
subjects affected / exposed	13 / 99 (13.13%)		
occurrences (all)	14		
Hyponatremia			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	6		
Investigations: other			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	13		
CRP increase			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	6		
Cardiac disorders			
Supraventricular arrhythmia			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	18		
Hypertension			
subjects affected / exposed	19 / 99 (19.19%)		
occurrences (all)	27		

Hypotension subjects affected / exposed occurrences (all)	5 / 99 (5.05%) 7		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Agitation subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Head/Headache subjects affected / exposed occurrences (all)	 11 / 99 (11.11%) 18 6 / 99 (6.06%) 8 9 / 99 (9.09%) 11 17 / 99 (17.17%) 19 19 / 99 (19.19%) 25		
Blood and lymphatic system disorders Hemoglobin subjects affected / exposed occurrences (all) Leukocytes subjects affected / exposed occurrences (all) Neutrophils subjects affected / exposed occurrences (all) Platelets subjects affected / exposed occurrences (all)	 85 / 99 (85.86%) 214 70 / 99 (70.71%) 192 42 / 99 (42.42%) 80 87 / 99 (87.88%) 234		
Gastrointestinal disorders Anorexia subjects affected / exposed occurrences (all) Constipation	 12 / 99 (12.12%) 16 		

subjects affected / exposed	33 / 99 (33.33%)		
occurrences (all)	51		
Diarrhea			
subjects affected / exposed	38 / 99 (38.38%)		
occurrences (all)	57		
Heartburn			
subjects affected / exposed	7 / 99 (7.07%)		
occurrences (all)	9		
Mucositis			
subjects affected / exposed	43 / 99 (43.43%)		
occurrences (all)	49		
Nausea			
subjects affected / exposed	57 / 99 (57.58%)		
occurrences (all)	109		
Vomiting			
subjects affected / exposed	30 / 99 (30.30%)		
occurrences (all)	47		
Pain Abdomen NOS			
subjects affected / exposed	17 / 99 (17.17%)		
occurrences (all)	19		
Pain Stomach			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	17		
Skin and subcutaneous tissue disorders			
Dermatology - other			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	12		
Injection site reaction			
subjects affected / exposed	24 / 99 (24.24%)		
occurrences (all)	45		
Pruritus			
subjects affected / exposed	9 / 99 (9.09%)		
occurrences (all)	10		
Rash			
subjects affected / exposed	27 / 99 (27.27%)		
occurrences (all)	45		

Renal and urinary disorders			
Fluid retention/edema			
subjects affected / exposed	42 / 99 (42.42%)		
occurrences (all)	68		
Musculoskeletal and connective tissue disorders			
Musculoskeletal - other			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	12		
Pain back			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	16		
Pain bone			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	7		
Pain Extremity/Limb			
subjects affected / exposed	9 / 99 (9.09%)		
occurrences (all)	16		
Pain: Joint			
subjects affected / exposed	8 / 99 (8.08%)		
occurrences (all)	12		
Infections and infestations			
Infection: Lip/perioral			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	12		
Febrile neutropenia			
subjects affected / exposed	43 / 99 (43.43%)		
occurrences (all)	73		
Infection: Catheter-related			
subjects affected / exposed	13 / 99 (13.13%)		
occurrences (all)	13		
Infection - other			
subjects affected / exposed	29 / 99 (29.29%)		
occurrences (all)	42		
Sepsis			
subjects affected / exposed	14 / 99 (14.14%)		
occurrences (all)	28		

Infection with grade 3/4 neutrophils subjects affected / exposed occurrences (all)	3 / 99 (3.03%) 3		
Infection with unknown ANC subjects affected / exposed occurrences (all)	11 / 99 (11.11%) 14		
Lung (pneumonia) subjects affected / exposed occurrences (all)	19 / 99 (19.19%) 29		
Infection: Urinary tract NOS subjects affected / exposed occurrences (all)	3 / 99 (3.03%) 3		

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