Clinical trial results:
Evaluation of Efficacy and Toxicity of Intensified Consolidation Therapy in AML Patients 60 Years

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2007-005806-29
Trial protocol	AT
Global end of trial date	21 January 2015

Results information

Result version number	v1 (current)
This version publication date	22 April 2016
First version publication date	22 April 2016
Summary attachment (see zip file)	Report final 18.12.2015 (Report final 18.12.2015.pdf)

Trial information

Trial identification

Sponsor protocol code	AKH-AML-0108

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medizinische Universität Wien
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
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	21 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Tolerability (number of cycles of consolidation therapy; toxicity) of intensified consolidation therapy in elderly AML patients
Adverse event profile

Protection of trial subjects:

The trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 July 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	17
From 65 to 84 years	46
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients were recruited in the participating centers located in Austria i.e. Medical Univerity of Vienna, Hospital Hietzing, Hospidal of the Elisabethinen Linz, Kaiser Franz Josef Hospidal Vienna, Donauspital Vienna between 17.07.2008 and 21.1.2015

Pre-assignment

Screening details:

All patients diagnosed with "de novo" AML aged ≥60 years eligible for intensive chemotherapy were screened

Pre-assignment period milestones

Number of subjects started	64
Number of subjects completed	64

Period 1

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

Arms

Arm title	Treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Daunorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intracavernous use
Dosage and administration details: 45mg/m², day 1-3 of Induction 1	
Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 mg/m², day 1-5 of Induction 1	
Investigational medicinal product name	Cytarabin
Investigational medicinal product code	
Other name	ARA-C
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg/m², days 1-7 of Induction 1;
2000mg/m², days 1-5 of Induction 3 and Consolidation 1,
2000mg/m², days 1, 3, 5 of Induction 2 and Consolidation 2, 3, and 4

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

Dosage and administration details:

12 mg/m² on days 3, 5 of Induction 2

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

30 mg/m² on days 1-5 of Induction 3 and Consolidation 1

Investigational medicinal product name	Pegfilgrastim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

6mg on the first day after chemotherapy

Number of subjects in period 1	Treatment
Started	64
Completed	64

Baseline characteristics

Reporting groups

Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	64	64	
Age categorical Units: Subjects			
Adults (18-64 years)	17	17	
From 65-84 years	46	46	
85 years and over	1	1	
Age continuous Units: years			
median	69.9		
full range (min-max)	60.1 to 85.2	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	39	39	

Subject analysis sets

Subject analysis set title	Overall
Subject analysis set type	Full analysis

Subject analysis set description:

All patients included in the study from start of chemotherapy to the end of follow up

Reporting group values	Overall		
Number of subjects	64		
Age categorical Units: Subjects			
Adults (18-64 years)	17		
From 65-84 years	46		
85 years and over	1		
Age continuous Units: years			
median	69.9		
full range (min-max)	60.1 to 85.2		
Gender categorical Units: Subjects			
Female	25		
Male	39		

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: -	
Subject analysis set title	Overall
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients included in the study from start of chemotherapy to the end of follow up	

Primary: AEs Consolidation 1

End point title	AEs Consolidation 1[1]
End point description:	
End point type	Primary
End point timeframe:	
Consolidation 1	

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: Because of the early termination, we only used descriptive statistical methods to describe the results of this trial.

Statistical analyses

No statistical analyses for this end point

Primary: AEs Consolidation 2

End point title	AEs Consolidation 2[2]
End point description:	
End point type	Primary
End point timeframe:	
Consolidation 2	

Notes:

[2] - 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: Because of the early termination, we only used descriptive statistical methods to describe the results of this trial.

Statistical analyses

No statistical analyses for this end point

Primary: AEs Consolidation 3

End point title	AEs Consolidation 3[3]

End point description:

End point type	Primary

End point timeframe:

Consolidation 3

Notes:

[3] - 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: Because of the early termination, we only used descriptive statistical methods to describe the results of this trial.

Statistical analyses

No statistical analyses for this end point

Primary: AEs Consolidation 4

End point title	AEs Consolidation 4[4]

End point description:

End point type	Primary

End point timeframe:

Consolidation 4

Notes:

[4] - 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: Because of the early termination, we only used descriptive statistical methods to describe the results of this trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Continuous complete remission

End point title	Continuous complete remission

End point description:

End point type	Secondary

End point timeframe:

Study period

Statistical analyses

No statistical analyses for this end point

Secondary: CR rate

End point title	CR rate

End point description:

End point type	Secondary

End point timeframe:

Induction phase

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse rate

End point title	Relapse rate

End point description:

End point type	Secondary

End point timeframe:
Study Period

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: number	25			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:
Study period

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: number				
median (full range (min-max))	1.1 (0 to 5.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Continuous complete remission

End point title	Continuous complete remission

End point description:

End point type	Secondary

End point timeframe:
Study period

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: number				
median (full range (min-max))	1.23 (0.15 to 5.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease free survival

End point title	Disease free survival

End point description:

End point type	Secondary

End point timeframe:
Study period

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: number				
median (full range (min-max))	1.23 (0.15 to 5.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of neutropenia Consolidation 1

End point title	Duration of neutropenia Consolidation 1

End point description:

End point type	Secondary

End point timeframe:
Consolidation 1

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of neutropenia Consolidation 2

End point title	Duration of neutropenia Consolidation 2

End point description:

End point type	Secondary

End point timeframe:
Consolidation 2

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of neutropenia Consolidation 3

End point title	Duration of neutropenia Consolidation 3

End point description:

End point type	Secondary

End point timeframe:
Consolidation 3

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of neutropenia Consolidation 4

End point title	Duration of neutropenia Consolidation 4

End point description:

End point type	Secondary

End point timeframe:

Consolidation 4

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of hospitalisation Consolidation 1

End point title	Duration of hospitalisation Consolidation 1

End point description:

End point type	Secondary

End point timeframe:

Consolidation 1

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of hospitalisation Consolidation 2

End point title	Duration of hospitalisation Consolidation 2

End point description:

End point type	Secondary

End point timeframe:
Consolidation 2

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of hospitalisation Consolidation 3

End point title	Duration of hospitalisation Consolidation 3

End point description:

End point type	Secondary

End point timeframe:
Consolidation 3

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of hospitalisation Consolidation 4

End point title	Duration of hospitalisation Consolidation 4

End point description:

End point type	Secondary

End point timeframe:
Consolidation 4

Statistical analyses

No statistical analyses for this end point

Secondary: GCS-F levels detectable up to day 14

End point title	GCS-F levels detectable up to day 14

End point description:

End point type	Secondary

End point timeframe:
Consolidation 1

Statistical analyses

No statistical analyses for this end point

Secondary: Age

End point title	Age

End point description:

End point type	Secondary

End point timeframe:
Study period

End point values	Treatment			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: years				
median (full range (min-max))	69.9 (60.1 to 85.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Study period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 64 (42.19%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Nervous system disorders			
Central nervous system haemorrhage			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cerebral haemorrhage			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dementia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurological decompensation			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death			

subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Disease progression				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Multi-organ failure				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Pyrexia				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Constipation				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ileus				

subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Diffuse alveolar damage				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Internal haemorrhage				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Renal and urinary disorders				
Haematinuria				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure acute				
subjects affected / exposed	2 / 64 (3.13%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Aspergilloma				
subjects affected / exposed	1 / 64 (1.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Clostridium colitis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 3		
Pneumonia			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	1 / 1		
Septic shock			
subjects affected / exposed	1 / 64 (1.56%)		
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	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 64 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	9 / 64 (14.06%)		
occurrences (all)	9		
Hypertension			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	5		
Hypotension			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	6		
Phlebitis			
subjects affected / exposed	9 / 64 (14.06%)		
occurrences (all)	9		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	17 / 64 (26.56%)		
occurrences (all)	23		
Mucosal inflammation			
subjects affected / exposed	21 / 64 (32.81%)		
occurrences (all)	30		
Oedema			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	18 / 64 (28.13%)		
occurrences (all)	24		
Pain assessment			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	7		
Peripheral swelling			

subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	13 / 64 (20.31%)		
occurrences (all)	18		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 64 (23.44%)		
occurrences (all)	15		
Dyspnoea			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	7		
Epistaxis			
subjects affected / exposed	15 / 64 (23.44%)		
occurrences (all)	21		
Oropharyngeal pain			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	7		
Pleural effusion			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	7		
Psychiatric disorders			
Depression			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	6		
Insomnia			
subjects affected / exposed	9 / 64 (14.06%)		
occurrences (all)	14		
Investigations			
C-reactive protein			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	7		
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	9		

Fall subjects affected / exposed occurrences (all)	11 / 64 (17.19%) 11		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	5 / 64 (7.81%) 5		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	18 / 64 (28.13%) 30		
Blood and lymphatic system disorders Febrile neutropenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	56 / 64 (87.50%) 134 8 / 64 (12.50%) 8		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	23 / 64 (35.94%) 35		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea haemorrhagic subjects affected / exposed occurrences (all) Haemorrhoids	4 / 64 (6.25%) 4 8 / 64 (12.50%) 10 11 / 64 (17.19%) 15 13 / 64 (20.31%) 18		

subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	33 / 64 (51.56%)		
occurrences (all)	76		
Vomiting			
subjects affected / exposed	13 / 64 (20.31%)		
occurrences (all)	22		
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	7		
Petechiae			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	11		
Rash			
subjects affected / exposed	14 / 64 (21.88%)		
occurrences (all)	16		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	6		
Cytarabine syndrome			
subjects affected / exposed	14 / 64 (21.88%)		
occurrences (all)	18		
Musculoskeletal pain			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	5		
Neck pain			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	6		
Pain in extremity			

subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	8		
Infections and infestations			
Candida infection			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	4		
Conjunctivitis			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	5		
Diarrhoea infectious			
subjects affected / exposed	14 / 64 (21.88%)		
occurrences (all)	23		
Febrile infection			
subjects affected / exposed	11 / 64 (17.19%)		
occurrences (all)	11		
Folliculitis			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	5		
Herpes virus infection			
subjects affected / exposed	17 / 64 (26.56%)		
occurrences (all)	22		
Infection			
subjects affected / exposed	37 / 64 (57.81%)		
occurrences (all)	78		
Oral herpes			
subjects affected / exposed	9 / 64 (14.06%)		
occurrences (all)	14		
Pneumonia			
subjects affected / exposed	19 / 64 (29.69%)		
occurrences (all)	21		
Urinary tract infection			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	6		
Fluid retention			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2009	Following substantials changes have been done: AEs have to be graded according to NCI CTC V3.0 Standardisation of prognostic factors over all sections Standardisation of secondary objectives over all sections Febrile neutropenia was defined as Fever >=38°C and ANC < 0.5G/L Analysing of KIT Mutation was added to the SCR procedure AML related findings were added to the SCR procedure HLA Typing was added to the SCR procedure Charlson Score moved from Induction 1 to the SCR visit Secondary objectives were deleted in section 10.1 MeDRA coding was added to the endpoints Wilcoxon signed rank test was added instead of Wilcoxon test (paired data) Typing errors were corrected Administration of Peg-Filgrastim in Induction 1 -3 at the discretion of the Principal Investigator Changes in the follow up period Mitoxantron was changed to Mitoxanthrone Daunorubicine was changed to Daunorubicin Change from „over" three hours to „for" three hours Change from „Seite" to „page"
30 September 2014	Following substantials changes have been done: Contact data have been changed from +43 1 40400 6085, Fax: +43 1 40400 4030 to Tel.: +43 1 40400 60850, Fax: +43 1 40400 40300 ANC <500 cells/µL has been changed to ANC <500 cells/µL or WBC < 1000 cells/µL (if ANC is not available) Follow up period has been changed from „In case of presence of a molecular marker, monitoring of this marker in the bm during the first 2 years after CR (in 3 months interval) Source data related to the follow up and follow up events will be documented in each center and will be collected and analyzed centrally (after recalling from centers) after 1, 3, and 5 years. Follow up should be performed 1 month after the end of treatment visit, and in an interval of 6 weeks or shorter for one year after the first follow up visit" to „In case of presence of a molecular marker, monitoring of this marker in the bm during the first 2 years after CR (in 6 months interval) Source data related to the follow up and follow up events will be documented in each center and will be collected and analyzed centrally (after recalling from centers) after 1, 3, and 5 years or until 15. Sep. 2014, whatever comes first. Follow up should be performed 1 month after end of treatment and in a six-week interval within the first year, thereafter at least every 6 months until 15. Sep. 2014" Section 9.2. has been amended: Inclusion of the sentence „The case report form (CRF) pages containing adverse event reporting by investigator, e.g. start date, stop date, frequency, severity, study relation and action taken for this event will serve as the source data."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 January 2015	On 21 January 2015 the clinical trial was prematurely terminated because of an extremly slow recruitment despite an already long recruitment period. It could not be expected that the planned number of subjects, who finished the trial acoording to the protocol, could be reached in a predicatble time period.There are a number of possible implications for the interpretation of the study because of these changes. Primarily because of the early termination not all planned endpoints – especially secondary - can be answered. Moreover, the statistical power of the results is markedly reduced. In case of no significant results, it cannot be excluded that these data would have become significant in case the total number of planned patients would have been included. On the other hand, borderline significant results are more questionable.	-

Notes:

Limitations and caveats

None reported