Clinical trial results:
Allogeneic stem cell transplantation for children, adolescents and young adults with relapsed or refractory AML
Multi Center Therapy Concept

Summary

EudraCT number	2007-004517-34
Trial protocol	DE CZ AT
Global end of trial date	19 January 2021

Results information

Result version number	v1 (current)
This version publication date	21 June 2025
First version publication date	21 June 2025

Trial information

Trial identification

Sponsor protocol code	AMLSCT-BFM2007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00606723
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.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	31 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 January 2021
Global end of trial reached?	Yes
Global end of trial date	19 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate whether stem cell transplantation (SCT) from a matched sibling donor (MSD) is equivalent to a matched unrelated donor (MUD) in second complete remission (CR2) (see statistics part).
• To evaluate whether "FLAMSA" increases survival as compared to a survival rate estimated from historical data (studies AML-BFM and Relapsed AML 2001/1) in children suffering from refractory AML or relapsed AML responding poorly to reinduction therapy.
• To evaluate whether HSCT from haploidentical donors for children having no matched donor increases survival as compared to a survival rate estimated from historical data (studies AML-BFM and Relapsed AML 2001/1) in children suffering from refractory AML or relapsed AML.

Protection of trial subjects:

The clinical trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with the standards of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 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: 7
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	Germany: 120
Worldwide total number of subjects	140
EEA total number of subjects	140

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)	26

Children (2-11 years)	65
Adolescents (12-17 years)	45
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligibility will be determined based upon the inclusion and exclusion criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group I - BuCyMel

Arm description:

Relapsed AML-patients with blast cell reduction to <20% before the second course of induction therapy or high-risk AML. These patients received conventional SCT.

Arm type	Experimental
Investigational medicinal product name	Busulfan
Investigational medicinal product code	
Other name	Busilvex
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Bodyweight < 9 kg: 4,0 mg/kg (daily dose), 8,0 mg/kg (cumulative dose)
Bodyweight 9-16 kg: 4,8 mg/kg (daily dose), 9,6 mg/kg (cumulative dose)
Day -7 to day -4 before stem cell transplantation

Investigational medicinal product name	Melphalan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

140 mg/m² i.v., day -1 before stem cell transplantation

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

60 mg/kg i.v., day -3 and day -2 before stem cell transplantation

Arm title	Group II - Flamsa

Arm description:

Patients with non response to frontline treatment of AML, patients with blast cells <20% before the second course of induction therapy who did not achieve a second remission and relapsed AMLpatients with blast cells > 20% before the second course of induction therapy. If these patients had a matched donor (MSD/MUD) they received SCT with “FLAMSA”.

Arm type	Experimental

Investigational medicinal product name	Amsacrin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

100 mg/m² i.v. as continuous infusion over 60 minutes
Children > 2 years: day -12 to day -9 before stem cell transplantation
Children < 2 years: day -13 to day -10 before stem cell transplantation

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

30 mg/m² i.v. as continuous infusion over 30 minutes
Children > 2 years: day -12 to day -9 before stem cell transplantation
Children < 2 years: day -13 to day -10 before stem cell transplantation

Investigational medicinal product name	AraC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

2 g/m² i.v. as continuous infusion over 2h
Children > 2 years: day -12 to day -9 before stem cell transplantaion
Children < 2 years: day -13 to day -10 before stem cell transplantaion

Investigational medicinal product name	Cyclophosphamid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

60/40 mg/kg i.v., day -4 and day -3 before stem cell transplantation

Investigational medicinal product name	Antithymocyte Globulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

20/10 mg/kg i.v., day -4 to day -2 before stem cell transplantation

Investigational medicinal product name	Busulfan
Investigational medicinal product code	
Other name	Busilvex
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Exclusively children < 2 years
Bodyweight < 9 kg: 4,0 mg/kg (daily dose)
Bodyweight 9-16 kg: 4,8 mg/kg (daily dose)
Daily dose divided in four infusions given over 2h each
Day -6 and day -5 before stem cell transplantation

Number of subjects in period 1	Group I - BuCyMel	Group II - Flamsa
Started	93	47
Completed	93	47

Baseline characteristics

Reporting groups	
Reporting group title	overall study

Reporting group description: -

Reporting group values	overall study	Total	
Number of subjects	140	140	
Age categorical Units: Subjects			
> 12 years	72	72	
< 12 years	68	68	
Gender categorical Units: Subjects			
Female	68	68	
Male	72	72	

End points

End points reporting groups

Reporting group title	Group I - BuCyMel

Reporting group description:

Relapsed AML-patients with blast cell reduction to <20% before the second course of induction therapy or high-risk AML. These patients received conventional SCT.

Reporting group title	Group II - Flamsa

Reporting group description:

Patients with non response to frontline treatment of AML, patients with blast cells <20% before the second course of induction therapy who did not achieve a second remission and relapsed AMLpatients with blast cells > 20% before the second course of induction therapy. If these patients had a matched donor (MSD/MUD) they received SCT with "FLAMSA".

Primary: Overall Survival rate

End point title	Overall Survival rate[1]

End point description:

Overall Survival was defined as the time from HCT to the date of last follow-up (censored time) or death. The Kaplan–Meier method was used to estimate survival rates; differences were compared using the log-rank test (two-sided).

End point type	Primary

End point timeframe:

four years

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: Survival rates were not compared between groups.

End point values	Group I - BuCyMel	Group II - Flamsa		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	47		
Units: percent				
arithmetic mean (standard error)	70 (± 5)	53 (± 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Eventfree sruvival rate

End point title	Eventfree sruvival rate

End point description:

Event-free survival (EFS) was defined as the time from HCT to the date of last follow-up (censored time) or first event. Events were relapse, secondary neoplasm, or death by any cause. OS was defined as the time from HCT to the date of last follow-up (censored time) or death. The Kaplan–Meier method was used to estimate survival rates; differences were compared using the log-rank test (two-sided).

End point type	Secondary

End point timeframe:

four years

End point values	Group I - BuCyMel	Group II - Flamsa		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	47		
Units: percent				
arithmetic mean (standard error)	61 (± 5)	49 (± 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: CIR - Cumulative incidence rate

End point title	CIR - Cumulative incidence rate

End point description:

Cumulative incidence functions for competing events were estimated according to Kalbfleisch and Prentice, and were compared with the Gray’s test.

End point type	Secondary

End point timeframe:

five and a half years

End point values	Group I - BuCyMel	Group II - Flamsa		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	47		
Units: Percentage protective dose				
arithmetic mean (standard error)	22 (± 4)	38 (± 7)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events which occur from the time point the patient meets the inclusion criteria for the trial up to the first 100 days after transplantation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	BuCyMel
Reporting group description: -	
Reporting group title	Haplo
Reporting group description: -	
Reporting group title	Flamsa

Reporting group description: -

Serious adverse events	BuCyMel	Haplo	Flamsa
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 99 (25.25%)	4 / 6 (66.67%)	15 / 35 (42.86%)
number of deaths (all causes)	13	2	8
number of deaths resulting from adverse events	13	2	8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia recurrent			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Leukaemia recurrent			
subjects affected / exposed	0 / 99 (0.00%)	2 / 6 (33.33%)	3 / 35 (8.57%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 3
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Venoocclusive disease			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vena cava thrombosis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (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
Multi-organ failure			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Pyrexia			
subjects affected / exposed	1 / 99 (1.01%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Acute graft versus host disease in skin			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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

Graft versus host disease			
subjects affected / exposed	2 / 99 (2.02%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Chronic graft versus host disease			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Reproductive system and breast disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Haemoptysis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	3 / 99 (3.03%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	2 / 3	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	5 / 99 (5.05%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Pulmonary oedema			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Engraft failure			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (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
Transplant failure			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	2 / 99 (2.02%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1

Cardiac arrest			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Cardiomyopathy			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neurotoxicity			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Encephalopathy			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
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			
Neutropenia			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Anaemia			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Pancreatic disorder			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Diarrhoea			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (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
Gastritis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Enterocolitis haemorrhagic			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Hepatic vein thrombosis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Venoocclusive liver disease			
subjects affected / exposed	4 / 99 (4.04%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	3 / 99 (3.03%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infections and infestations			
Infection			
subjects affected / exposed	2 / 99 (2.02%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			

subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter sepsis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Epstein-Barr virus infection			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Pseudomonas infection			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Toxoplasmosis			
subjects affected / exposed	0 / 99 (0.00%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster pneumonia			

subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Viral haemorrhagic cystitis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (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
Viral sepsis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Zygomycosis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (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
Septic shock			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2

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

Non-serious adverse events	BuCyMel	Haplo	Flamsa
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 99 (100.00%)	6 / 6 (100.00%)	35 / 35 (100.00%)
Cardiac disorders			
Inotropic support with catecholamines			
subjects affected / exposed	18 / 99 (18.18%)	1 / 6 (16.67%)	8 / 35 (22.86%)
occurrences (all)	18	1	8
Shortening fraction < 25 %			
subjects affected / exposed	7 / 99 (7.07%)	0 / 6 (0.00%)	3 / 35 (8.57%)
occurrences (all)	7	0	3
Anti-arrhythmic therapy			
subjects affected / exposed	3 / 99 (3.03%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences (all)	3	0	2
Nervous system disorders			
Seizure			
subjects affected / exposed	3 / 99 (3.03%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences (all)	3	0	2
Central nervous system haemorrhage			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Leukoencephalopathy			
subjects affected / exposed	0 / 99 (0.00%)	1 / 6 (16.67%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	4 / 99 (4.04%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	4	0	1
Gastrointestinal haemorrhage			
subjects affected / exposed	8 / 99 (8.08%)	0 / 6 (0.00%)	1 / 35 (2.86%)
occurrences (all)	8	0	1
Respiratory, thoracic and mediastinal disorders			
Radiologic changes and/or oxygen support			
subjects affected / exposed	37 / 99 (37.37%)	2 / 6 (33.33%)	15 / 35 (42.86%)
occurrences (all)	37	2	15
Mechanical ventilation			

subjects affected / exposed	14 / 99 (14.14%)	1 / 6 (16.67%)	2 / 35 (5.71%)
occurrences (all)	14	1	2
Hepatobiliary disorders			
Relevant bilirubine elevation			
subjects affected / exposed	15 / 99 (15.15%)	1 / 6 (16.67%)	3 / 35 (8.57%)
occurrences (all)	15	1	3
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	1 / 99 (1.01%)	0 / 6 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Hemodialysis or hemofiltration			
subjects affected / exposed	8 / 99 (8.08%)	0 / 6 (0.00%)	2 / 35 (5.71%)
occurrences (all)	8	0	2
Relevant creatinine elevation			
subjects affected / exposed	8 / 99 (8.08%)	0 / 6 (0.00%)	3 / 35 (8.57%)
occurrences (all)	8	0	3
Infections and infestations			
Infection occurred			
subjects affected / exposed	61 / 99 (61.62%)	2 / 6 (33.33%)	21 / 35 (60.00%)
occurrences (all)	61	2	21

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2010	-Addition of chapter 6.1 Recruitment and 6.2 Visit Schedule - Adjustment of chapter 7. Inclusion and 8. Exclusion criteria -Changes in chapter 9. Stratification
10 January 2012	-Changes in primary objectives, inclusion and exclusion criteria - Elongation of the conditioning between 18 and 7 days before transplantation (6.2 Visit Schedule) -Specification of inclusion criteria -Removal of the exclusion criterion: Severely impaired functional performance (Karnofsky score < 70%, Lansky play score < 70%) -Adjustment of chapter 9. Stratification and addition of point 6. Patients with primarily very high risk AML in CR1 (defined by the following aberrations: 12p, monosomy 7, t(4;11), t(6;11), t(6;9), t(7;12), t(9;22), t(8;16), and WT1mut/FLT-ITD or AML as secondary malignancy (not MDS-related)).
07 September 2012	- Addition of Drug safety: Monitoring and documentation of adverse events and adverse reactions as well as serious adverse events and serious adverse reactions. - Changes in the definition (chapter 23.1) of adverse events, adverse reaction, Serious adverse event / Serious adverse reaction, Suspected unexpected serious adverse reaction as well as addition of Documentation of adverse events / serious adverse events - Adjustment of chapter 23.2. Reporting of serious adverse events - Changes in chapter 23.3. Annual safety reports and deletion of section development safety update report
11 June 2014	- 1.5-years prolongation of recruiting - Adjustment of inclusion criteria - Adjustment of stratification points 5. and 6. - Increase of the patient number in treatment group I - Changes of the statistical consideration of group III - Addition of stopping rules
17 November 2014	In Group I inclusion criteria were changed in "only if < 12 years old"
03 January 2019	-Changes due to a sponsor change

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
15 October 2014	According to §11 and §13 of the national GCP guideline, recruitment of patients ≥12 years group I was temporary stopped on 15 October 2014 and the AML SCT BFM 2007 protocol was substantially amended (protocol version 10.0 of 17.11.2014).	01 December 2014

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31578451