Clinical trial results:
A Randomized Phase III study comparing conventional chemotherapy to low dose total body irradiation-based conditioning and hematopoietic cell transplantation from related and unrelated donors as consolidation therapy for older Patients with AML in first Complete Remission.

Summary

EudraCT number	2007-003514-34
Trial protocol	DE NL FR AT
Global end of trial date	31 August 2020

Results information

Result version number	v1 (current)
This version publication date	24 October 2021
First version publication date	24 October 2021
Summary attachment (see zip file)	HCT vs CT in elderly AML final report 1.0 (HCTvsCT_final_report_final1.0_2021-08-25_blackened.pdf)

Trial information

Trial identification

Sponsor protocol code	HCTvs.CTelderlyAML

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00766779
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The European Society for Blood and Marrow Transplantation
Sponsor organisation address	Rijnsburgerweg 10, Leiden, Netherlands, 2333 AA
Public contact	hctvsct@zks.uni-leipzig.de, Leipzig University, hctvsct@zks.uni-leipzig.de
Scientific contact	hctvsct@zks.uni-leipzig.de, Leipzig University, hctvsct@zks.uni-leipzig.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	25 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2020
Global end of trial reached?	Yes
Global end of trial date	31 August 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate LFS after allogeneic HCT in AML/RAEB in CR using matched or unrelated donors in comparison to conventional chemotherapy

Primary endpoints
- Leukemia free survival (LFS)

Protection of trial subjects:

An independent data monitoring committee was installed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 January 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	Netherlands: 33
Country: Number of subjects enrolled	Germany: 79
Country: Number of subjects enrolled	Switzerland: 13
Worldwide total number of subjects	125
EEA total number of subjects	112

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)	37

From 65 to 84 years	88
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

245 Patients were recruited registered for the trial from 11.01.2011 until 31.08.2017 in the participating trial sites in Germany, the Netherlands, France, Switzerland, Austria and Australia.

Pre-assignment

Screening details:

A total of 125 patients proceeded to randomisation.

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	stem cell transplant

Arm description:

hematopoietic stem cell transplantation after low dose total body irradiation-based conditioning

Arm type	Experimental
Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per day: 30 mg/m2 mg/m2, days -4, -3, -2

Investigational medicinal product name	Ciclosporin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion, Capsule, soft + tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Start day -3 until day 84, then taper

Investigational medicinal product name	Mycophenolatmofetil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion, Capsule
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

Per day: 45 mg/kg mg/kg, related donor: day 0 until day 28, unrelated donor: day 0 until day 28, then reduction of 500mg / 14 days

Investigational medicinal product name	hematopoietic stem cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The peripheral blood stem cell (PBSC) graft should contain at least 4 x 106 /kg CD34 and 3 x 108 /kg CD3+ cells. Infusion on day 0.

Arm title	non stem cell transplant

Arm description:

Patients randomized in Arm B were scheduled to receive further consolidation according to an upfront specified trial site protocol.

Arm type	standard of care
Investigational medicinal product name	Mitoxantron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per day: 10 mg/m2, days 1 and 2

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

Dosage and administration details:

Per day: 500 mg/m2, days 1, 3 and 5

Number of subjects in period 1	stem cell transplant	non stem cell transplant
Started	83	42
Completed	66	35
Not completed	17	7
Relapse	2	2
miscellaneous reasons	5	-
donor not available	3	-
Withdrawal	3	3
Morbidity	4	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	stem cell transplant
Reporting group description:	
hematopoietic stem cell transplantation after low dose total body irradiation-based conditioning	
Reporting group title	non stem cell transplant
Reporting group description:	
Patients randomized in Arm B were scheduled to receive further consolidation according to an upfront specified trial site protocol.	

Primary: Leukaemia free survival (LFS)

End point title	Leukaemia free survival (LFS)[1]
End point description:	
End point type	Primary
End point timeframe:	
5 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: The trial was stopped prematurely. For further description see the attached trial synopsis.	

End point values	stem cell transplant	non stem cell transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	42		
Units: whole	83	42		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Before Amendment 1 adverse events were reported from between the first study-related procedure (i.e. screening) until 30 days post the last study treatment. After Amendment 1 the reporting period changed to day 0 (start of trial therapy) until day 100.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	stem cell transplant
Reporting group description: -	
Reporting group title	non stem cell transplant
Reporting group description: -	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Please see the list of AEs related and not related to the IMP in the trial synopsis, uploaded together with the posting of this results report.

Serious adverse events	stem cell transplant	non stem cell transplant	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 66 (10.61%)	1 / 35 (2.86%)	
number of deaths (all causes)	4	0	
number of deaths resulting from adverse events			
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage neonatal			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Splenic haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			

Death			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 66 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Human herpesvirus 6 infection			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	

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

Non-serious adverse events	stem cell transplant	non stem cell transplant	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 66 (0.00%)	0 / 35 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2011	Complete Revision
03 July 2013	Amendment
07 November 2013	Amendment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported