



## Clinical trial results:

### 10-day decitabine, fludarabine and 2 Gray TBI as conditioning strategy for poor and very poor risk AML in CR1

#### Summary

EudraCT number	2014-000400-99
Trial protocol	NL BE
Global end of trial date	01 October 2020

#### Results information

Result version number	v1 (current)
This version publication date	01 March 2022
First version publication date	01 March 2022

#### Trial information

##### Trial identification

Sponsor protocol code	PLMA34
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02252107
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Radboud university medical center
Sponsor organisation address	P.O. Box 9101, Nijmegen, Netherlands, 6500 HB
Public contact	Afdeling Hematologie Trialcoördinat, Radboud university medical center, Datacentrum@HEMAT.umcn.nl
Scientific contact	Afdeling Hematologie Trialcoördinat, Radboud university medical center, Datacentrum@HEMAT.umcn.nl

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	01 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2020
Global end of trial reached?	Yes
Global end of trial date	01 October 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the feasibility (safety and efficacy) of addition of 10-day decitabine to the standard Seattle non-myeloablative conditioning regimen (3 days fludarabine 30 mg/m<sup>2</sup> + 2 Gray TBI) prior to allogeneic HCT in poor and very poor risk AML patients in CR1.

Safety will be assessed by adverse events and laboratory parameters; efficacy will be assessed by (decrease of) relapse rate at 12 months (fixed time point) after last-patient-in.

Protection of trial subjects:

We closely monitored for adverse events and also installed a data and safety management board (DSMB)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 43
Country: Number of subjects enrolled	Belgium: 3
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	33
From 65 to 84 years	13
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Initially, 56 patients were included. There were 10 screening failures, resulting in 46 patients starting and completing the study.

### Period 1

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

### Arms

Arm title	9/10 and 10/10 matched donor
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Arm description:

Patients with a 10/10 matched donor received only decitabine, fludarabine and TBI. Patients with a 9/10 mismatched donor received all products indicated below in the arm specification

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

Dosage and administration details:

Decitabine to be dissolved in 100 ml NaCl 0.9%. Dose/day is 20 mg/m<sup>2</sup>. Infusion for 1 hour on days -11 through -2.

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

Dosage and administration details:

Fludarabine to be dissolved in 50 ml NaCl 0.9%. Dose/day is 30 mg/m<sup>2</sup>. Infusion for 0.5 hour on days -4, -3 and -2.

Investigational medicinal product name	Total body irradiation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for...
Routes of administration	Other use

Dosage and administration details:

2 gray on day -1.

Investigational medicinal product name	Anti Thymocyte Globulin ATG (rabbit)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

ATG (rabbit) to be dissolved in 500 ml NaCl 0.9%. Dose/day is 2 mg/kg. Infusion for 10 hours on days -8, -7, -6 and -5.

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

Dosage and administration details:

Methylprednison dissolved in 250 ml NaCl 0.9%. Dose/day is 2 mg/kg. Infusion for 0.5 hours on days -8, -7, -6 and -5.

Investigational medicinal product name	Clemastine
Investigational medicinal product code	
Other name	Tavegil
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg on days -8, -7, -6 and -5.

<b>Number of subjects in period 1</b>	9/10 and 10/10 matched donor
Started	46
Completed	46

## Baseline characteristics

### Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	46	46	
Age categorical			
Units: Subjects			
Age continuous			
all adult patients (18 years or older)			
Units: years			
median	60		
full range (min-max)	23 to 74	-	
Gender categorical			
both male and female allowed			
Units: Subjects			
Female	22	22	
Male	24	24	
Type of disease			
Units: Subjects			
De novo AML	41	41	
Secondary AML	5	5	
WHO classification 2008			
Units: Subjects			
AML with recurrent genetic abnormalities	4	4	
AML with myelodysplasia related changes	15	15	
Therapy-related myeloid neoplasms	4	4	
AML, not otherwise specified	22	22	
Myeloid sarcoma	1	1	
Disease status at start of conditioning			
Units: Subjects			
Complete remission (CR)	29	29	
Incomplete remission (CRi)	17	17	
Donor type			
Units: Subjects			
Matched 10/10	43	43	
Mismatched 9/10	3	3	

## End points

### End points reporting groups

Reporting group title	9/10 and 10/10 matched donor
Reporting group description: Patients with a 10/10 matched donor received only decitabine, fludarabine and TBI. Patients with a 9/10 mismatched donor received all products indicated below in the arm specification	

### Primary: Relapse at 1-year after the transplantation procedure

End point title	Relapse at 1-year after the transplantation procedure <sup>[1]</sup>
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End point description:

End point type	Primary
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End point timeframe:

1-year after the transplantation procedure

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: No comparison was made. A 1-sided alpha of 5% was used.

<b>End point values</b>	9/10 and 10/10 matched donor			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: percentage	23			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Non-relapse mortality

End point title	Non-relapse mortality
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End point description:

Time to death in CR or non-relapse related mortality (NRM) is defined as the time between the date of complete remission and the date of death in CR (i.e. without a documentation of relapse). For subjects who remain alive and did not relapse, NRM will be censored on the date of last visit/contact with disease assessments. The follow-up of patients who relapsed will be censored at the date of relapse. For the computation of the cumulative incidence of death without relapse, relapse will be considered as a competing risk. Defined according to ELN criteria.

End point type	Secondary
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End point timeframe:

Within the first year post allo HCT

<b>End point values</b>	9/10 and 10/10 matched donor			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: percentage	11			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description:	
Defined according to ELN criteria	
End point type	Secondary
End point timeframe:	
One year	

<b>End point values</b>	9/10 and 10/10 matched donor			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: Percentage	70			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Relapse-free survival (RFS)

End point title	Relapse-free survival (RFS)
End point description:	
Defined according to ELN criteria.	
End point type	Secondary
End point timeframe:	
One year	

<b>End point values</b>	9/10 and 10/10 matched donor			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: Percentage	66			

### Statistical analyses

No statistical analyses for this end point

### Secondary: GVHD-free survival (GRFS)

End point title	GVHD-free survival (GRFS)
End point description: GRFS was defined as surviving the first 12 months after allo HCT without relapse and without grade III-IV aGVHD and/or severe cGVHD.	
End point type	Secondary
End point timeframe: One year	

<b>End point values</b>	9/10 and 10/10 matched donor			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: Percentage	45			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From date first included patient, until 1 year after the last included patient

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.0
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### Reporting groups

Reporting group title	9/10 and 10/10 matched donor
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Reporting group description:

Patients with a 10/10 matched donor received only decitabine, fludarabine and TBI. Patients with a 9/10 mismatched donor received all products indicated below in the arm specification

Serious adverse events	9/10 and 10/10 matched donor		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 46 (26.09%)		
number of deaths (all causes)	18		
number of deaths resulting from adverse events	2		
Nervous system disorders			
Vasovagal reaction			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea and vomiting			

subjects affected / exposed	2 / 46 (4.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Thoracic pain			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Encephalitis			
subjects affected / exposed	1 / 46 (2.17%)		
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 %

<b>Non-serious adverse events</b>	9/10 and 10/10 matched donor		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 46 (26.09%)		
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Cardiac disorders			
Heart failure			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
General disorders and administration site conditions			
Insomnia			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Immune system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	3		
Graft versus host disease			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences (all)	2		
Pain at right flank			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Hepatobiliary disorders			
Blood bilirubin increased			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences (all)	2		
ALT increased			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
AST increased			

subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1		
Respiratory, thoracic and mediastinal disorders Idiopathic pneumonia syndrome subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1		
Renal and urinary disorders Creatinine increased subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1		
Product issues Take failure subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	Additional description: RS virus 1 / 46 (2.17%) 1		
Metabolism and nutrition disorders Anorexia nervosa subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/33824442>