Clinical trial results:
Prophylactic application of donor-derived central memory T lymphocytes (TCM) after allogeneic HSCT to prevent infectious complications

Summary

EudraCT number	2015-001522-41
Trial protocol	DE
Global end of trial date	30 December 2022

Results information

Result version number	v1 (current)
This version publication date	03 April 2024
First version publication date	03 April 2024

Trial information

Trial identification

Sponsor protocol code	PACT2014-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Würzburg
Sponsor organisation address	Josef-Schneider-Str. 2, Würzburg, Germany, 97080
Public contact	Hematology/Oncology, University Hospital Wuerzburg - Departement of Medicine II, 0049 93120144500, grigoleit_g@ukw.de
Scientific contact	Hematology/Oncology, University Hospital Wuerzburg - Departement of Medicine II, 0049 93120144500, grigoleit_g@ukw.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	20 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2022
Global end of trial reached?	Yes
Global end of trial date	30 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the toxicity and feasibility of prophylactic administration of donor derived central memory T Cells after T cell depleted allo-SCT

Protection of trial subjects:

Subject will be enrolled in a strict sequential order with a one month safety period between treatment of first patient and treatment of second patient. If first treatment of third patient will be given, first patient will receive his third treatment. Afterwards patients can be enrolled simultaneously.
After the eighth patient received last treatment all data available till then will be reviewed by DSMB to assess whether side effect related to study medication or significant GvHD occurred.
Based on limited data regarding the risk of GvHD for which TCM account within the TM population, we consider the TCM compart- ment for safety reasons as potentially alloreactive and treat it in analogy to the naive T cell compartment.

Background therapy:

Adoptive T cell therapy , antigen-specific T cells . donor-derived central memory T lymphocytes (TCM).

Evidence for comparator:

not applicable

Actual start date of recruitment	23 December 2015
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	Germany: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	9
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient entry: 28-APR-2016,
Last patient entry: 23-JUL-2020

Pre-assignment

Screening details:

All patients will be documented in the Screening Log. In case a patient will not be included, this will be documented with the specific reason for non-inclusion. Each patient included into the study is uniquely identified in the study by a combination of study code, his/her center and patient number (e.g. PACT-WU01).

Pre-assignment period milestones

Number of subjects started	21[1]
Intermediate milestone: Number of subjects	Screening-Phase: 21
Number of subjects completed	16

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 1
Reason: Number of subjects	Adverse event, serious fatal: 2
Reason: Number of subjects	Protocol deviation: 2

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 2 protocol deviations, 2 serious fatal events and 1 physician decision to exclude the patient

Period 1

Period 1 title	Treatment and Follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

no blinding

Arms

Arm title	Donor-derived central memory T lymphocytes (TCM) after allogen

Arm description:

The first patient group will be treated with 5x103 T cells/kg bw at day 30 (+/- 5) and escalating doses of 1x104 T cells/kg bw and 5x104 T cells/kg bw at day 60 (+/- 5) and day 90 (+/- 5). If no significant GVHD occurs, the second patient group will be treated with 5x104 T cells/kg bw at day 30 (+/- 5) and escalating doses of 1x105 T cells/kg bw and 5x105 T cells/kg bw at day 60 (+/- 5) and day 90 (+/- 5).

Arm type	Experimental
Investigational medicinal product name	Donor-derived central memory T lymphocytes (TCM) after allogenic HSCT
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

The first patient group will be treated with 5x103 T cells/kg bw at day 30 (+/- 5) and escalating doses of 1x104 T cells/kg bw and 5x104 T cells/kg bw will be administered atday
60 (+/- 5) and day 90 (+/- 5) when no side effects will have occurred after the previous transfer.

The second patient group (15 pts) will be treated with 5x104 T cells/kg bw at day 30 (+/- 5) and will be administered escalating doses of 1x105 T cells/kg bw and 5x105 T cells/kg bw at day 60 (+/- 5) and day 90 (+/- 5) when no side effects will have occurred after the previous transfer.

Number of subjects in period 1	Donor-derived central memory T lymphocytes (TCM) after allogen
Started	16
Completed	9
Not completed	7
Adverse event, serious fatal	7

Baseline characteristics

Reporting groups

Reporting group title	Treatment and Follow-up

Reporting group description: -

Reporting group values	Treatment and Follow-up	Total	
Number of subjects	16	16	
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			
Age at time of informed consent			
Units: years			
arithmetic mean	62.6		
standard deviation	± 8.7	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	15	15	
Diagnosis at inclusion			
Diagnosis for inclusion in the study: AML: Acute myeloid leukemia MDS: Myelodysplastic syndrome			
Units: Subjects			
AML	3	3	
MDS	13	13	

Subject analysis sets

Subject analysis set title	Intention-to-treat population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who received at least one dose of donor derived TCM.

Subject analysis set title	Efficacy-evaluable subpopulation
Subject analysis set type	Per protocol

Subject analysis set description:

all patients from the ITT population with sampled EDTA blood for immunological monitoring over a period of at least eight weeks after the infusion of the first dose of TCM

Reporting group values	Intention-to-treat population	Efficacy-evaluable subpopulation	
Number of subjects	16	12	
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			
Age at time of informed consent			
Units: years arithmetic mean standard deviation	 62.6 ± 8.7	 62.8 ± 9.7	
Gender categorical Units: Subjects			
Female Male	1 15	1 11	
Diagnosis at inclusion			
Diagnosis for inclusion in the study: AML: Acute myeloid leukemia MDS: Myelodysplastic syndrome			
Units: Subjects			
AML MDS	3 13	3 9	

End points

End points reporting groups

Reporting group title	Donor-derived central memory T lymphocytes (TCM) after allogen

Reporting group description:

The first patient group will be treated with 5x103 T cells/kg bw at day 30 (+/- 5) and escalating doses of 1x104 T cells/kg bw and 5x104 T cells/kg bw at day 60 (+/- 5) and day 90 (+/- 5). If no significant GVHD occurs, the second patient group will be treated with 5x104 T cells/kg bw at day 30 (+/- 5) and escalating doses of 1x105 T cells/kg bw and 5x105 T cells/kg bw at day 60 (+/- 5) and day 90 (+/- 5).

Subject analysis set title	Intention-to-treat population
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All patients who received at least one dose of donor derived TCM.

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Primary: Cumulative incidence of acute or chronic overall GvHD

End point title	Cumulative incidence of acute or chronic overall GvHD

End point description:

cumulative incidence of acute or chronic GVHD overall grade ≥3 or higher within 3 months after infusion of the last dose of TCM
the incidence of acute GVHD > overall grade II occurring between the time of infu- sion of the T cell prod As the incidence of acute GVHD > overall grade II occurring between the time of infusion of the T cell product and 6 months after the alloHSCT

End point type	Primary

End point timeframe:

6 months

End point values	Donor-derived central memory T lymphocytes (TCM) after allogen	Intention-to-treat population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	16	16		
Units: integer	0	0		

Statistical analyses

Statistical analysis title	Estimation og GvHD rate

Statistical analysis description:

A sample size of 25 patients is sufficiently for providing statistical evidence that our study procedure ensures an acceptable rate of success for an adaptive transfer. For this we plan a one sample test for single-stage phase II clinical trials. Then a sample size of 25 patients is needed in order to test the null hypothesis H0 that the underlying true success probability is <=0.26 [largest proportion of success that

implies that the treatment does not warrant further study] against the alterna

Comparison groups	Donor-derived central memory T lymphocytes (TCM) after allogen v Intention-to-treat population
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	event rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.285
Variability estimate	Standard deviation

Notes:

[1] - Estimation for an event rate

Secondary: At least one Successful TCM transfers assessed by routine immunological monitoring

End point title	At least one Successful TCM transfers assessed by routine immunological monitoring

End point description:

End point type	Secondary

End point timeframe:

A successful transfer is defined as:

The percentage of circulating T cells with a TCM phenotype with one of the described specific- ities doubles during eight weeks after infusion of the first, second or third dose as compared to the percentage befor

End point values	Donor-derived central memory T lymphocytes (TCM) after allogen	Intention-to-treat population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	16	12		
Units: 2				
no	3	0		
yes	13	12		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

9 months

Adverse event reporting additional description:

All adverse events reported spontaneously by the subject or observed by the investigatoror will be recorded. Investigators will be required to report to the Sponsor all adverse events occurring during the clinical trial, including the post-treatment follow-up period. Serious ad- verse events must be reported to the Sponsor within 24 hours of knowle

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	TCM treated

Reporting group description:

All patients in the study treated with TCM cells

Serious adverse events	TCM treated		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 16 (81.25%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	7		
General disorders and administration site conditions			
All events			
subjects affected / exposed	13 / 16 (81.25%)		
occurrences causally related to treatment / all	0 / 22		
deaths causally related to treatment / all	0 / 7		

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

Non-serious adverse events	TCM treated		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 16 (93.75%)		
General disorders and administration site conditions			
All events			
subjects affected / exposed	15 / 16 (93.75%)		
occurrences (all)	175		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 December 2018	early dose escalation and sample size re-assessment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported