Clinical trial results:
PSCT16 Study: Vaccination with minor histocompatibility antigenloaded donor DC vaccines to boost graft-versus-tumor immunity after allogeneic stem cell transplantation
PSCT19 Study: Vaccination with PD-L1/L2-silenced minor histocompatibility antigen-loaded donor DC vaccines to boost graft-versus-tumor immunity after allogeneic stem cell transplantation (a phase I/II study)

Summary

EudraCT number	2012-002879-34
Trial protocol	NL
Global end of trial date	06 October 2020

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	PSCT16 & PSCT19

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboud University Medical Center Nijmegen
Sponsor organisation address	Geert Grooteplein Zuid 8, Nijmegen, Netherlands, 6500 HB
Public contact	Trialbureau Hematologie-Oncologie, Radboud University Nijmegen Medical Centre, 31 243614794, studies.hemat@radboudumc.nl
Scientific contact	Trialbureau Hematologie-Oncologie, Radboud University Nijmegen Medical Centre, 31 243614794, studies.hemat@radboudumc.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	06 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2020
Global end of trial reached?	Yes
Global end of trial date	06 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective PSCT16:
-to evaluate the safety and toxicity of pre-emptive administration of donor DCs electroporated with mRNA encoding hematopoietic-restricted MiHA.
-to evaluate the capability and strength (i.e. % MiHA-specific T cells within total CD8+ T population) of MiHA mRNA-loaded donor DC to induce in vivo expansion of CD8+ memory T cells against hematopoietic-restricted MiHA.
-to evaluate the immune response to KLH
Primary Objective PSCT19:
The study is designed as a phase I/II study in 10 patients who had undergone HLA-matched allogeneic SCT:
-to evaluate the toxicity of pre-emptive administration of PD-L1/L2-silenced donor DCs electroporated with mRNA encoding hematopoietic-restricted MiHA.
-to evaluate the capability and strength (i.e. % MiHA-specific T cells within total CD8+ T population) of MiHA mRNA-loaded donor DC to induce in vivo expansion of CD8+ memory T cells against hematopoietic-restricted MiHA.
-to evaluate the immune response to KLH

Protection of trial subjects:

The responsible investigator will ensure that this study is conducted in agreement with either the Declaration of Helsinki (Tokyo, Venice, Hong Kong, Somerset West and Edinburgh amendments), or the laws and regulations of the country whichever provides the greatest protection of the patient.
The design of this study follows current views of the European Medicine Agency (EMA) for Advanced Medicinal Therapy Products (AMTP) in general and for Cellular Advanced Therapeutics (CAT) in particular.
The protocol has been written, and the study will be conducted according to the guidelines for Good Clinical Practice and Good Manufacturing Practice issued by the European Union.
The protocol has been approved by the Central Committee on Research Involving Human Subjects

Background therapy:

No background therapy was given

Evidence for comparator:

Not applicable

Actual start date of recruitment	03 June 2013
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	Netherlands: 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)	13
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Prior to allogeneic stem cell transplantation HLA-A2+ and HLA-B7+ recipient donor pairs were asked permission for genotyping for MiHA mismatches for HA-1, LRH-1 and ARHGDIB. Patients with MiHA mismatches in the graft-versus-tumor direction, who met the inclusion criteria were asked informed consent for this dendritic cell vaccination study

Pre-assignment

Screening details:

For the pilot study (PSCT16), 17 patients were screened, of whom 4 included. One patient was withdrawn because he did not fulfill the criteria. For the PSCT19 study, 48 patients were screened, of whom 12 included. The screening criteria can be found in the protocols.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pilot PSCT16 study

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MiHA mRNA-electroporated mature DCs
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20x10^6 MiHA mRNA-electrocoporated mature DCs were infused on day 0, 14 and 28

Arm title	PSCT19 study

Arm description: -

Arm type	Experimental
Investigational medicinal product name	monocyte-derived, PD-L1/L2-silenced donor DCs electroporated with mRNA encoding hematopoietic-restricted MiH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Monocyte-derived, PD-L1/L2-silenced donor DCs electroporated with mRNA encoding hematopoietic-restricted MiH, 2,5x10^5/kg, intravenous on day 0, 14, and 28

Number of subjects in period 1	Pilot PSCT16 study	PSCT19 study
Started	4	12
Completed	4	12

Period 2	
Period 2 title	During treatment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Pilot PSCT16 study

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MiHA mRNA-electroporated mature DCs
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20x10^6 MiHA mRNA-electrocoporated mature DCs were infused on day 0, 14 and 28

Arm title	PSCT19 study

Arm description: -

Arm type	Experimental
Investigational medicinal product name	monocyte-derived, PD-L1/L2-silenced donor DCs electroporated with mRNA encoding hematopoietic-restricted MiH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Monocyte-derived, PD-L1/L2-silenced donor DCs electroporated with mRNA encoding hematopoietic-restricted MiH, 2,5x10^5/kg, intravenous on day 0, 14, and 28

Number of subjects in period 2[1]	Pilot PSCT16 study	PSCT19 study
Started	3	10
Completed	3	10

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 16 subjects were included in the study, 3 patients did not start the study
*In the PSCT16 study one patient did not meet inclusion criteria so this patient was not treated
*In the PSCT19 study one patient dit not start treatment because the donor did nog give consent for monocyte aferesis,
*In the PSCT19 study one patient did not have the right HLA type

Period 3

Period 3 title	After the end of treatment (Follow-up)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Pilot PSCT16 study

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MiHA mRNA-electroporated mature DCs
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20x10^6 MiHA mRNA-electrocoporated mature DCs were infused on day 0, 14 and 28

Arm title	PSCT19 study

Arm description: -

Arm type	Experimental
Investigational medicinal product name	monocyte-derived, PD-L1/L2-silenced donor DCs electroporated with mRNA encoding hematopoietic-restricted MiH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Monocyte-derived, PD-L1/L2-silenced donor DCs electroporated with mRNA encoding hematopoietic-restricted MiH, 2,5x10^5/kg, intravenous on day 0, 14, and 28

Number of subjects in period 3	Pilot PSCT16 study	PSCT19 study
Started	3	10
Completed	3	10

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	14	14	
From 65-84 years	2	2	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	5	5	
Male	11	11	
Disease			
Primary diagnosis of patients included in the study			
Units: Subjects			
Non Hodgkin lymphoma	5	5	
Acute myeloid leukemia	4	4	
Chronic myelomonocytic leukemia	2	2	
Hodgkin lymphoma	1	1	
Chronic myeloid leukemia	1	1	
Acute lymphoblastic leukemia	1	1	
Myelodysplastic syndrome	1	1	
Multiple myeloma	1	1	

End points

End points reporting groups

Reporting group title	Pilot PSCT16 study
Reporting group description: -	
Reporting group title	PSCT19 study
Reporting group description: -	
Reporting group title	Pilot PSCT16 study
Reporting group description: -	
Reporting group title	PSCT19 study
Reporting group description: -	
Reporting group title	Pilot PSCT16 study
Reporting group description: -	
Reporting group title	PSCT19 study
Reporting group description: -	

Primary: Toxicity - Adverse events

End point title	Toxicity - Adverse events[1]

End point description:

Adverse events > grade 2 according to CTCAE in PSCT16 trial and adverse events > grade 1 to CTCAE in PSCT 19 trial
Serious adverse events

End point type	Primary

End point timeframe:

Patiënts were screened for adverse events during study visits.
The study visits were: prestudy, day 0, day 7, day 14, day 21, day 28, day 42, day 63 and day 84.

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: This is a phase 1 trial, so adverse events are described and not compared between the two groups.

End point values	Pilot PSCT16 study	PSCT19 study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[2]	10[3]		
Units: Adverse events				
Fever	0	6		
Flu like symptoms	0	5		
Fatigue	0	2		
Musculoskeletal pain	0	2		
Viral infections	0	3		
Cough	0	1		
Hypotension	0	1		
Incomplete spinal cord injury	0	1		
Malaise	0	2		
Graft-versus-host disease	0	0		

Notes:

[2] - Adverse events > CTCEA grade 2 (according to study protocol)

[3] - Adverse events > CTCAE grade 1

Statistical analyses

No statistical analyses for this end point

Primary: GVHD

End point title	GVHD[4]

End point description:

End point type	Primary

End point timeframe:

Patiënts were screened for adverse events during study visits.
The study visits were: prestudy, day 0, day 7, day 14, day 21, day 28, day 42, day 63 and day 84.

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: Statistical analysis is not applicable for this endpoint. Graft-versus-host disease dit not occur in any of the reporting groups.

End point values	Pilot PSCT16 study	PSCT19 study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	10		
Units: Graft-versus-host disease				
Graft-versus-host disease	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Immunological response of MiHA CD8+ T cells

End point title	Immunological response of MiHA CD8+ T cells[5]

End point description:

End point type	Primary

End point timeframe:

The amount of MiHA specific CD8+ cells was counted prestudy and on day 0, 7, 14, 21, 28, 35, 63 and 84

Notes:

[5] - 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: This analysis is still ongoing

End point values	Pilot PSCT16 study	PSCT19 study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Increase in MiHA specific CD8+ T cells				

Notes:

[6] - This analysis is still ongoing

[7] - This analysis is still ongoing

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events reported spontaneously by the subject or observed by the investigator or his staff occuring until 84 days after the first DC vaccination will be recorded in the eCRF.

Assessment type	Non-systematic

Dictionary used

Dictionary name	NCI-CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Pilot PSCT16 study

Reporting group description:

All patients included in the study who received at least one dose of treatment.
AE's of CTCAE grade 1 and 2 are not considered AE's in this protocol.

Reporting group title	PSCT19 study

Reporting group description:

AEs of CTCAE grade 1 are not considered adverse events in this study

Serious adverse events	Pilot PSCT16 study	PSCT19 study	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Pilot PSCT16 study	PSCT19 study	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	10 / 10 (100.00%)	
Vascular disorders			
Hypotension	Additional description: Hypotension grade 3 on study day 23 after third vaccination during one day.		
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Incomplete spinal cord injury	Additional description: Due to progression of multiple myeloma		
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Fever	Additional description: > grade 1 fever		
subjects affected / exposed	0 / 3 (0.00%)	6 / 10 (60.00%)	
occurrences (all)	0	6	
Flu like symptoms	Additional description: Flu like symptoms > grade 1		
subjects affected / exposed	0 / 3 (0.00%)	5 / 10 (50.00%)	
occurrences (all)	0	5	
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Viral gastro-enteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough > grade 1		
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 January 2018	Amendement concering PSCT19 trial -Hodgkin lymphoma has been added to inclusion criteria -Patiënts can be included after tapering of immune suppression instead of after tapering of ciclosporin A -Adverse events of grade 2 or higher will be described in the CRF -Donors will have a 12 liter apheresis instead of a 9 liter apheresis -Follow up will be performed on day 35 instead of day 42
04 July 2019	Patients with myeloprolifertive neoplasms can be included in the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported