



## Clinical trial results:

### Myeloid and plasmacytoid blood dendritic cells for immunotherapy of stage III melanoma patients

#### Summary

EudraCT number	2010-023757-11
Trial protocol	NL
Global end of trial date	14 April 2021

#### Results information

Result version number	v1 (current)
This version publication date	29 December 2022
First version publication date	29 December 2022

#### Trial information

##### Trial identification

Sponsor protocol code	myDC/pDC in stage III melanoma
-----------------------	--------------------------------

##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02574377
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	RadboudUMC
Sponsor organisation address	Geert Grooteplein Zuid, NIJMEGEN, Netherlands, 6525 GA
Public contact	Radboudumc, Radboud University Medical Centre Nijmegen, 0031 243617600, jolanda.devries@radboudumc.nl
Scientific contact	Radboudumc, Radboud University Medical Centre Nijmegen, 0031 243617600, jolanda.devries@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	21 April 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 April 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

This is an interventional study and the primary objective is the biodistribution and the immunogenicity of single and combined pDC and myDC vaccination.

Protection of trial subjects:

This study will be conducted in accordance with the principles of the Declaration of Helsinki (October 9th, 2004) and the Medical Research Involving Human Subjects Act (WMO; December 1st, 1999). All serious adverse events (SAE) and suspected unexpected serious adverse reactions (SUSAR) will be reported via ToetsingOnline to the CCMO that approved the protocol, according to the requirements of the CCMO. All adverse events will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist.

Background therapy:

N.a.

Evidence for comparator:

N.a.

Actual start date of recruitment	01 October 2015
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: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	12
From 65 to 84 years	5
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

17 patients were included in the study, of which 15 were evaluable. Two patients were replaced because of rapid disease progression.

### Period 1

Period 1 title	Treatment phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	myDC

Arm description:

Patients received myeloid dendritic cell vaccinations

Arm type	Experimental
Investigational medicinal product name	Ex vivo labeled peptide-loaded blood DC product: myDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralymphatic use

Dosage and administration details:

Vaccines consisted of 2-5 million autologous myDC

<b>Arm title</b>	p-DC
------------------	------

Arm description:

Patients received plasmacytoid dendritic cell vaccinations

Arm type	Experimental
Investigational medicinal product name	Ex vivo labeled peptide-loaded blood DC product: pDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralymphatic use

Dosage and administration details:

Vaccines consisted of 1-3 million autologous pDC

<b>Arm title</b>	pDC/myDC
------------------	----------

Arm description:

Patients received combined plasmacytoid and myeloid dendritic cell vaccinations

Arm type	Experimental
Investigational medicinal product name	Ex vivo labeled peptide-loaded blood DC product: myDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralymphatic use

Dosage and administration details:

Vaccines consisted of 2-5 million autologous myDC

Investigational medicinal product name	Ex vivo labeled peptide-loaded blood DC product: pDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralymphatic use

Dosage and administration details:

Vaccines consisted of 1-3 million autologous pDC

<b>Number of subjects in period 1</b>	myDC	p-DC	pDC/myDC
Started	5	7	5
Completed	4	3	2
Not completed	1	4	3
Consent withdrawn by subject	-	-	1
Disease progression	1	4	2

## Baseline characteristics

### Reporting groups

Reporting group title	myDC
Reporting group description:	
Patients received myeloid dendritic cell vaccinations	
Reporting group title	p-DC
Reporting group description:	
Patients received plasmacytoid dendritic cell vaccinations	
Reporting group title	pDC/myDC
Reporting group description:	
Patients received combined plasmacytoid and myeloid dendritic cell vaccinations	

Reporting group values	myDC	p-DC	pDC/myDC
Number of subjects	5	7	5
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	4	4
From 65-84 years	1	3	1
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	1	4	3
Male	4	3	2

Reporting group values	Total		
Number of subjects	17		
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)	12		
From 65-84 years	5		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	8		
Male	9		

## End points

### End points reporting groups

Reporting group title	myDC
Reporting group description: Patients received myeloid dendritic cell vaccinations	
Reporting group title	p-DC
Reporting group description: Patients received plasmacytoid dendritic cell vaccinations	
Reporting group title	pDC/myDC
Reporting group description: Patients received combined plasmacytoid and myeloid dendritic cell vaccinations	
Subject analysis set title	HLA-A2.1, HLA-AL or HLA-B35 positive patients
Subject analysis set type	Full analysis
Subject analysis set description: Patients for whom matching MHC-dextramers were available to assess antigen-specificity of T-cells	
Subject analysis set title	HLA-A2.1 positive patients with sufficient SKILS
Subject analysis set type	Full analysis
Subject analysis set description: Patients for whom both matching MHC-multimers were available and sufficient outgrowth of skin-infiltrating lymphocytes (SKILs) after DTH-challenge.	
Subject analysis set title	Patients with sufficient SKILs regardless of HLA-haplotype
Subject analysis set type	Full analysis
Subject analysis set description: Patients for whom sufficient SKILs were available to assess antigen-specificity of T-cells with an HLA-independent method	
Subject analysis set title	Patients evaluable for HRQoL
Subject analysis set type	Full analysis
Subject analysis set description: Patients for whom an HRQoL questionnaire was completed at baseline and week 26	

### Primary: Antigen-specific T-cells (in DTH-challenged sites) detected by MHC-multimer staining

End point title	Antigen-specific T-cells (in DTH-challenged sites) detected by MHC-multimer staining <sup>[1]</sup>
End point description: Number of patients with demonstrable antigen-specific T-cells cultured from skin biopsies in a DTH-challenged site	
End point type	Primary
End point timeframe: After the first vaccination cycle	

#### 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: For this endpoint, no between-group comparison with statistical analysis was performed.



<b>End point values</b>	HLA-A2.1 positive patients with sufficient SKILS			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: Number of patients with a response	4			

## Statistical analyses

No statistical analyses for this end point

### Primary: Antigen-specific T-cells (in PBMCs) detected by MHC-multimer staining

End point title	Antigen-specific T-cells (in PBMCs) detected by MHC-multimer staining <sup>[2]</sup>
End point description:	Number of patients with demonstrable antigen-specific T-cells derived from PBMCs
End point type	Primary
End point timeframe:	After the first vaccination cycle

Notes:

[2] - 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: For this endpoint, no between-group comparison with statistical analysis was performed.

<b>End point values</b>	HLA-A2.1, HLA-AL or HLA-B35 positive patients			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: Patients with a response	7			

## Statistical analyses

No statistical analyses for this end point

### Primary: Antigen-specific T-cells (in DTH-challenged sites) assessed in an HLA-independent assay

End point title	Antigen-specific T-cells (in DTH-challenged sites) assessed in an HLA-independent assay <sup>[3]</sup>
End point description:	Number of patients with demonstrable antigen-specific T-cells cultured from skin biopsies in a DTH-challenged site, assessed by measuring IFN $\gamma$ - response after coculturing with peptide-loaded PBMCs.
End point type	Primary
End point timeframe:	After the first vaccination cycle

Notes:

[3] - 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: For this endpoint, no between-group comparison with statistical analysis was performed.

<b>End point values</b>	Patients with sufficient SKILs regardless of HLA-haplotype			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: Number of patients with a response	9			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Recurrence-free survival

End point title	Recurrence-free survival
End point description: Recurrence-free survival in months. For groups where median survival is not reached at the date of data-cutoff, the median duration of follow-up is given. This was the case for the pDC/myDC group.	
End point type	Secondary
End point timeframe: Long-term follow-up	

<b>End point values</b>	myDC	p-DC	pDC/myDC	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	5	
Units: months				
median (full range (min-max))	17.1 (3.5 to 60.8)	47.7 (9.2 to 61.5)	57.5 (3.3 to 61.0)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: HRQoL - global health status

End point title	HRQoL - global health status
End point description: As measured by EORTC-QLQ-C30 questionnaire	
End point type	Secondary
End point timeframe: After 26 weeks compared to baseline	

<b>End point values</b>	Patients evaluable for HRQoL			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Difference in HRQoL score from baseline				
arithmetic mean (standard deviation)	15 ( $\pm$ 16)			

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were reported from inclusion onwards throughout the treatment phase.

Adverse event reporting additional description:

Adverse events of at least grade 3 or grade 1–2 and occurring in more than 1 patient are shown.

Assessment type	Non-systematic
-----------------	----------------

### Dictionary used

Dictionary name	CTCAE
-----------------	-------

Dictionary version	4.0
--------------------	-----

### Reporting groups

Reporting group title	Overall
-----------------------	---------

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)		
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	5		
Blood and lymphatic system disorders			
Hypocalcaemia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Hypophosphataemia			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	5		

Eosinophil count increased subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		
Hypernatraemia subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		
Hypokalaemia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	11 / 15 (73.33%) 11		
Pain	Additional description: Skin pain at administration site		
subjects affected / exposed occurrences (all)	4 / 15 (26.67%) 4		
Injection site reaction subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		
Hepatobiliary disorders			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Full article can be found on <a href="https://www.tandfonline.com/doi/full/10.1080/2162402X.2021.2015113">https://www.tandfonline.com/doi/full/10.1080/2162402X.2021.2015113</a>
--

Notes:

---

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30465182>