Clinical trial results:
An exploratory study: Dendritic cells for immunotherapy of metastatic endometrial cancer patients

Summary

EudraCT number	2018-004467-31
Trial protocol	NL
Global end of trial date	01 March 2021

Results information

Result version number	v1 (current)
This version publication date	25 October 2022
First version publication date	25 October 2022

Trial information

Trial identification

Sponsor protocol code	DECENDO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04212377
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radboud University Medical Center
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands, 6525 GA
Public contact	Dept of Tumor Immunology, Radboud University Medical Center, 0031 24 361 76 00, dcvaccinatie.til@radboudumc.nl
Scientific contact	Dept of Tumor Immunology, Radboud University Medical Center, 0031 24 361 76 00, dcvaccinatie.til@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	01 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2021
Global end of trial reached?	Yes
Global end of trial date	01 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this exploratory study is to show immunologic efficacy of tumor-peptide-loaded natural DC in mEC patients. The immune-monitoring will include: a) functional response and dextramer analysis of DTH infiltrating lymphocytes against tumor peptides, b) type I IFN gene expression in PBMC shortly after vaccination, and c) proliferative, effector cytokine- and humoral responses to keyhole limpet hemocyanin (KLH), an immunogenic protein providing T cell help.

Protection of trial subjects:

Dendritic cell vaccination is a safe and generally well tolerated treatment. Common side effects are flu-like symptoms and local reaction at the injection side. Patients were allowed to use paracetamol to alleviate these symptoms if needed. Adverse events were monitored throughout the study. All serious adverse events (SAE) and suspected unexpected serious adverse reactions (SUSAR) were reported via ToetsingOnline to 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. A progress and safety report was submited to the CCMO on a yearly basis.

Background therapy:

All patients in the trial received chemotherapy with carboplatin (AUC 4) and paclitaxel (90 mg/m2) in a weekly schedule for six cycles. If patients demonstrated at least stable disease, they received three more cycles of carboplatin (AUC 5) and paclitaxel (175 mg/m2) in a three-weekly schedule along with DC vaccination.

Evidence for comparator:

N.a. in this single-arm study.

Actual start date of recruitment	08 April 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	2
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place between April 8th 2019 and July 16th 2020.

Pre-assignment

Screening details:

One screening failure occurred, due to rapid disease progression, becoming evident between signing of informed consent and the first study procedure.

Period 1

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

Arms

Arm title	nDC vaccination

Arm description:

Patients in the study received a total of six peptide- and KLH-pulsed nDC-vaccinations in addition to the platinum-based chemotherapy regimen as described earlier.

Arm type	Experimental
Investigational medicinal product name	Autologous tumor antigen peptide-, and KLH-loaded blood-derived natural dendritic cell
Investigational medicinal product code	ENDO-DC
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intralymphatic use

Dosage and administration details:

A total of six vaccinations (3 per round) of nDC, each consisting of 5 million cells/dose

Number of subjects in period 1	nDC vaccination
Started	7
Completed	7

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	7	7	
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 in years at the time of inclusion			
Units: years			
median	65		
full range (min-max)	58 to 71	-	
Gender categorical			
All patients included were female.			
Units: Subjects			
Female	7	7	
Male	0	0	

End points

End points reporting groups

Reporting group title	nDC vaccination

Reporting group description:

Patients in the study received a total of six peptide- and KLH-pulsed nDC-vaccinations in addition to the platinum-based chemotherapy regimen as described earlier.

Primary: KLH-response after nDC-vaccination

End point title	KLH-response after nDC-vaccination[1]

End point description:

In vitro proliferation of patient-derived PBMCs after exposure to KLH, as measured by a standard 3H-thymidine incorporation assay. Cutoff for positive response was defined as a two-fold increase over KLH-stimulated proliferation in baseline PBMCs.

End point type	Primary

End point timeframe:

After first round of nDC vaccinations

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 comparative analysis was performed for the primary endpoints in this single-arm study.

End point values	nDC vaccination			
Subject group type	Reporting group			
Number of subjects analysed	5[2]			
Units: Subjects with a KLH-response				
Responders	2			
Non-responders	3			

Notes:

[2] - Only patients who received at least one nDC vaccination were included in this analysis.

Statistical analyses

No statistical analyses for this end point

Primary: Tumor peptide-specific immune response

End point title	Tumor peptide-specific immune response[3]

End point description:

Tumor peptide specificity was assessed in T-cells obtained from a vaccine-challenged site (DTH) by measuring different effector cytokines in response to tumor-specific peptides.

End point type	Primary

End point timeframe:

After the first and second round of nDC-vaccinations

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: No comparative analysis was performed for the primary endpoints in this single-arm study.

End point values	nDC vaccination			
Subject group type	Reporting group			
Number of subjects analysed	3[4]			
Units: Number of patients with a response				
Responder	1			
Non-responder	2			

Notes:

[4] - A sufficient amount of T-cells for this analysis were available for three patients.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were

Adverse event reporting additional description:

Adverse events were collected during each clinic visit by the treating physician and reported in the electronic patient file.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	nDC vaccination

Reporting group description:

Patients in the study received a total of six peptide- and KLH-pulsed nDC-vaccinations in addition to the platinum-based chemotherapy regimen as described earlier.

Serious adverse events	nDC vaccination		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Intrathoracic bleeding	Additional description: Intrathoracic bleeding as complication of an image-guided biopsy.		
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diverticulitis	Additional description: Mild diverticulitis warranting admission to a hospital only because of quick diagnostic workup prior to planned start of chemotherapy.		
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	nDC vaccination		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)		
General disorders and administration site conditions			
Flu-like symptoms			
subjects affected / exposed	4 / 7 (57.14%)		
occurrences (all)	4		
Any chemotherapy-related adverse events			
subjects affected / exposed	6 / 7 (85.71%)		
occurrences (all)	6		

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

None reported