



## Clinical trial results:

### T-cell therapy in combination with checkpoint inhibitors for patients with advanced ovarian-, fallopian tube- and primary peritoneal cancer.

#### Summary

EudraCT number	2017-002179-24
Trial protocol	DK
Global end of trial date	02 June 2020

#### Results information

Result version number	v1 (current)
This version publication date	03 July 2020
First version publication date	03 July 2020
Summary attachment (see zip file)	Summary of results (Summary of trial results.docx)

#### Trial information

##### Trial identification

Sponsor protocol code	GY1721
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03287674
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	National Center for Cancer Immune Therapy (CCIT-DK)
Sponsor organisation address	Borgmester Ib Juuls Vej 25C, Herlev, Denmark, 2730
Public contact	National Center for Cancer Immune Therapy, National Center for Cancer Immune Therapy, 0045 38683868, anders.kverneland@regionh.dk
Scientific contact	National Center for Cancer Immune Therapy, National Center for Cancer Immune Therapy, 0045 4538683868, anders.kverneland@regionh.dk

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	16 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2020
Global end of trial reached?	Yes
Global end of trial date	02 June 2020
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To evaluate toxicity (according to CTCAE version 4.0) and feasibility.

Protection of trial subjects:

All side effects were treated in accordance with best clinical practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
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	Denmark: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	6
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

All patients were recruited from Danish oncology centers between 2017-2018.

### Pre-assignment

Screening details:

Patients eligible for therapy were screening at Herlev Hospital according to in- and exclusion criteria described in the protocol.

### Period 1

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

### Arms

<b>Arm title</b>	TILs and checkpoint inhibition
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Arm description:

Ipilimumab, Cyclophosphamide, Fludarabine, TILs, Nivolumab, IL-2

Arm type	Experimental
Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

60 mg/kg daily for 2 days. Day -7 and -6 before TIL infusion

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg once, 2 weeks before tumor removal

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m<sup>2</sup> daily (max 50 mg) for 5 days. At day -5 to -1 before TIL infusion

Investigational medicinal product name	Tumor infiltrating lymphocytes
Investigational medicinal product code	
Other name	TILs, REP-TILs
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Typically 25-100 billion autologous T-cells expanded ex vivo from patients's own metastasis

Investigational medicinal product name	Interleukin-2
Investigational medicinal product code	
Other name	IL-2, aldesleukin
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

2 MIE daily for 14 days. Starting at day +1 after TIL infusion

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg every 14 days until 4 doses. Starting on day -2 before TILs.

<b>Number of subjects in period 1</b>	<b>TILs and checkpoint inhibition</b>
Started	6
7 patients recruited	6
6 patients treated	6
6 patients discontinued after therapy	6
Completed	6

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment time
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Reporting group description: -

Reporting group values	Treatment time	Total	
Number of subjects	6	6	
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)	6	6	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	0	0	

## End points

### End points reporting groups

Reporting group title	TILs and checkpoint inhibition
Reporting group description: Ipilimumab, Cyclophosphamide, Fludarabine, TILs, Nivolumab, IL-2	

### Primary: Feasibility

End point title	Feasibility <sup>[1]</sup>
End point description: Successful ex vivo expansion and re-infused into the patient	
End point type	Primary
End point timeframe: Oct-2017 to July 2018	

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: The clinical trial is very small with only 6 participants. No consideration was given to statistical power. Statistical analyses involve non-parametric comparisons.

End point values	TILs and checkpoint inhibition			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Successful TIL therapy				
Successful ex vivo expansion	6			
Successful re-infusion	6			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall response rate

End point title	Overall response rate
End point description: Best overall response according to RECIST 1.1.	
End point type	Secondary
End point timeframe: 3-9 months after TIL infusion	

<b>End point values</b>	TILs and checkpoint inhibition			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: No. subjects				
Complete response	0			
Partial response	1			
Stable disease	5			
Progressive disease	0			

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:  
from recruitment to discontinuation from protocol

Adverse event reporting additional description:  
CTCAE 4.0.

Non-serious event are only reported if grade>2

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	TIL treated group
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Reporting group description: -

Serious adverse events	TIL treated group		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Red blood cell count decreased	Additional description: anemia following discharge		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis	Additional description: Following ipilimumab		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory symptom	Additional description: Serious respiratory deficiency following TIL infusion		



subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cystitis	Additional description: In relation to JJ catheter		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	TIL treated group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
General disorders and administration site conditions			
Performance status decreased			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	6		
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	6		
red blood cell reduced			
subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	7		
Platelet count decreased			
subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	6		

Immune system disorders			
Infection	Additional description: Infetion during immune suspression		
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Renal and urinary disorders			
Hyponatraemia			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Endocrine disorders			
Thyroiditis	Additional description: immune mediated		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infections and infestations			
Fever	Additional description: Fever>40		
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		

## **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