



Clinical trial results: T cell therapy for patients with advanced Ovarian Cancer Summary

EudraCT number	2015-000530-30
Trial protocol	DK
Global end of trial date	03 April 2017

Results information

Result version number	v1 (current)
This version publication date	24 May 2018
First version publication date	24 May 2018

Trial information

Trial identification

Sponsor protocol code	GY1508
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02482090
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Inge Marie Svane
Sponsor organisation address	Herlev Ringvej 75, Herlev, Denmark, 2730
Public contact	Inge Marie Svane, Center for Cancer Immune Therapy, 0045 38682131, inge.marie.svane@regionh.dk
Scientific contact	Inge Marie Svane, Center for Cancer Immune Therapy, 0045 38682131, inge.marie.svane@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 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2017
Global end of trial reached?	Yes
Global end of trial date	03 April 2017
Was the trial ended prematurely?	No

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:

Not relevant

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 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	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)	4
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were enrolled in Herlev, Denmark between October 2015 to November 2016.

Pre-assignment

Screening details:

Eleven patients had tissue removed for TIL product generation. Five patients did not receive treatment due to: benign surgical biopsy for TIL production (n = 1); unsuccessful TIL expansion (n = 1); clinical deterioration (n = 3)

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	TIL in ovarian cancer
------------------	-----------------------

Arm description:

All patients receive the same treatment. All patients are hospitalized during treatment (approximately 3 weeks) and receive treatment only once.

Stem Cells are harvested a minimum of 3 weeks before treatment for potential later use if the patients are having difficulties recovering from the lymphodepleting chemotherapy.

The patients are admitted to hospital day -8 and receive lymphodepleting chemotherapy (cyclophosphamide and fludarabine= on day -7 to day -1.

The TILs are infused on day 0 and Interleukin-2 therapy is administered on day 0 to day 5.

Interleukin-2 is administered in an i.v. continuous decrescendo regimen starting approximately 6 hours after TIL infusion with a duration of approximately 5 days.

Stem Cells can be administered after treatment if needed.

Arm type	Experimental
Investigational medicinal product name	Tumor-infiltrating lymphocytes
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

5x10e9 to 2x10e11 cells

Number of subjects in period 1	TIL in ovarian cancer
Started	6
Completed	6

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	6	6	
Age categorical			
They were 50-65 years old (median 59 years) with CA-125 levels ranging from 10-4320 kU/L (median 214) and FIGO stage IIIC (n = 4) and IV (n = 2) disease, and had received two to six prior treatment regimens (median three)			
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)	4	4	
From 65-84 years	2	2	
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	TIL in ovarian cancer
Reporting group description:	
All patients receive the same treatment. All patients are hospitalized during treatment (approximately 3 weeks) and receive treatment only once.	
Stem Cells are harvested a minimum of 3 weeks before treatment for potential later use if the patients are having difficulties recovering from the lymphodepleting chemotherapy.	
The patients are admitted to hospital day -8 and receive lymphodepleting chemotherapy (cyclophosphamide and fludarabine= on day -7 to day -1.	
The TILs are infused on day 0 and Interleukin-2 therapy is administered on day 0 to day 5.	
Interleukin-2 is administered in an i.v. continuous decrescendo regimen starting approximately 6 hours after TIL infusion with a duration of approximately 5 days.	
Stem Cells can be administered after treatment if needed.	

Primary: Tolerability and feasibility

End point title	Tolerability and feasibility ^[1]
End point description:	
There was no unexpected adverse events related to treatment.	
End point type	Primary
End point timeframe:	
October 2015 - April 2017	
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 was a pilot study treating patients with ovarian cancer with TIL therapy. No unexpected toxicity was observed in six patients and thus, treatment was deemed tolerable and feasible.	

End point values	TIL in ovarian cancer			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Events	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
End point description:	
Median overall survival at the time of data analysis	
End point type	Secondary

End point timeframe:
October 2015 - April 2017

End point values	TIL in ovarian cancer			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: months	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival
End point description:	Median progression-free survival
End point type	Secondary
End point timeframe:	October 2015-April 2017

End point values	TIL in ovarian cancer			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: months	6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

October 2015 - April 2017

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	21.0
--------------------	------

Reporting groups

Reporting group title	TIL in ovarian cancer
-----------------------	-----------------------

Reporting group description:

All patients receive the same treatment. All patients are hospitalized during treatment (approximately 3 weeks) and receive treatment only once.

Stem Cells are harvested a minimum of 3 weeks before treatment for potential later use if the patients are having difficulties recovering from the lymphodepleting chemotherapy.

The patients are admitted to hospital day -8 and receive lymphodepleting chemotherapy (cyclophosphamide and fludarabine= on day -7 to day -1.

The TILs are infused on day 0 and Interleukin-2 therapy is administered on day 0 to day 5.

Interleukin-2 is administered in an i.v. continuous decrescendo regimen starting approximately 6 hours after TIL infusion with a duration of approximately 5 days.

Stem Cells can be administered after treatment if needed.

Serious adverse events	TIL in ovarian cancer		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Vascular disorders			
Venous thrombosis	Additional description: Deep venous thrombosis grade 2. Unrelated to treatment.		
subjects affected / exposed	2 / 6 (33.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever	Additional description: Fever grade 2 led to prolongation of hospitalization.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal			

disorders			
Dyspnoea	Additional description: Dyspnoea grade 4. Related to treatment. Is a known adverse reaction to study treatment.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	TIL in ovarian cancer		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Investigations			
Hyponatraemia	Additional description: Hyponatraemia grade 3. Related to treatment		
subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	6		
Hypophosphataemia	Additional description: Hypophosphataemia grade 3. Related to treatment.		
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	5		
Hypokalaemia	Additional description: Hypokalaemia grade 3. Related to treatment.		
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	5		
Nervous system disorders			
Confusional state	Additional description: Confusional state grade 3. Related to treatment.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hallucination	Additional description: Hallucination grade 3. Treatment related.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Performance status decreased	Additional description: Performance status decreased to 3. Related to treatment		
subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	6		
Fever	Additional description: Fever grade 3.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Febrile neutropenia	Additional description: Febrile neutropenia grade 3. Related to study treatment.		

subjects affected / exposed	6 / 6 (100.00%)		
occurrences (all)	6		
Fatigue	Additional description: Fatigue grade 3. Related to treatment		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash maculo-papular	Additional description: Grade 3. Related to treatment.		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

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.

Pilot trial with only 6 trial subjects.

Notes: