Clinical trial results:
Cabazitaxel in patients with Recurrent Ovarian Cancer after failure of standard therapy- A phase II trial

Summary

EudraCT number	2015-002296-18
Trial protocol	DK
Global end of trial date	05 December 2018

Results information

Result version number	v1 (current)
This version publication date	19 November 2020
First version publication date	19 November 2020

Trial information

Trial identification

Sponsor protocol code	CaTo-ROC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02560337
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vejle Hospital
Sponsor organisation address	Beriderbakken 4, Vejle, Denmark,
Public contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.dk
Scientific contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.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	13 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to investigate the effect of cabazitaxel in patients with recurrent ovarian cancer.

Protection of trial subjects:

Infusions and monitorering were performed according to institutional guidelines.

Anamnesis, clinical examination, blood pressure, quality of life and toxicity assessments were performed before each cycle.

Biochemistry with hematology, CA-125, creatinine, Na, K, Mg, Ca, bilirubin, ALAT, alkaline phosphatase, KFNT, LDH was measured before each cycle and hematology weekly for the first cycle.

CT of thorax/abdomen was performed after every 3rd cycle.

Background therapy:

Premedication:
Iv Clemastin 2 mg
Iv Solu-Medrol 40 mg
Iv Ranitidin 50 mg

Antiemetic prophylaxis was given according to institutional guidelines.

Primary prophylaxis with granulocyte colony-stimulating factor (G-CSF) was prescribed to all patients on day two of each cycle to reduce the risk of febrile neutropenia.

Evidence for comparator: -

Actual start date of recruitment	24 September 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: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

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)	18
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

- Danish women with ovarian cancer
- Enrollment from September 2015 until november 2018

Pre-assignment

Screening details:

- Platinum resistant ovarian cancer with at least two previous cytostatic regimens or platinum-refractory disease defined as progression while receiving the last line of platinum based therapy or within 4 weeks of last platinum dose.
Screened patients: 39

Period 1

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

Blinding implementation details:

Not blinded

Arms

Arm title	Cabazitaxel

Arm description: -

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

Dosage and administration details:

25 mg/m2 administered as a one hour intravenous infusion on day 1 of 3-week cycles.

Number of subjects in period 1	Cabazitaxel
Started	26
Completed	26

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	26	26	
Age categorical			
Platinum resistant ovarian cancer with at least two previous cytostatic regimens or platinum-refractory disease			
Units: Subjects			
Adults (18-64 years)	18	18	
From 65-84 years	8	8	
Age continuous			
Platinum resistant ovarian cancer with at least two previous cytostatic regimens or platinum-refractory disease			
Units: years			
median	61		
full range (min-max)	38 to 77	-	
Gender categorical			
Women with ovarian cancer			
Units: Subjects			
Female	26	26	
Danish women with ovarian cancer			
Units: Subjects			
Recurrent platinum resistant ovarian cancer	26	26	

End points

End points reporting groups

Reporting group title	Cabazitaxel

Reporting group description: -

Primary: The fraction of patients alive and without progression after three months of treatment with cabazitaxel

End point title	The fraction of patients alive and without progression after three months of treatment with cabazitaxel[1]

End point description:

The fraction of patients alive and without progression after three months of treatment with cabazitaxel

End point type	Primary

End point timeframe:

3 months

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: In this program it is not possible to use statistical analyses for fraction of patients alive at three months.

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Number of patients				
Number of patients	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival

End point title	Progression free survival

End point description:

Progression free survival (PFS)

End point type	Secondary

End point timeframe:

Months

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Months				
median (confidence interval 95%)				
PFS	3.9 (1.9 to 4.4)			

Attachments (see zip file)	PFS Eudract..pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Response rate

End point title	Response rate

End point description:

Patients were evaluable by both Response Evaluation Criteria in Solid Tumors (RECIST1.1) and by GCIG modified criteria for CA125 response,

End point type	Secondary

End point timeframe:

NA

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Percent				
RECIST	4			
GCIG modified criteria for CA125 response,	12			

Attachments (see zip file)	Respons rate Eudract..pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival (OS)

End point type	Secondary

End point timeframe:

Months

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Months				
median (confidence interval 95%)	8.4 (5.1 to 11.0)			

Attachments (see zip file)	OS Eudract..pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity of the treatment.

End point title	Toxicity of the treatment.

End point description:

To investigate the potential toxicity of the treatment.
Toxicities were reported and graded using the National Cancer Institute's Common Toxicity Criteria (NCI-CTC) version 4.0, year 2010.

End point type	Secondary

End point timeframe:

During treatment

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Grade	26			

Attachments (see zip file)	Toxicities Eudract..pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life

End point title	Quality of life

End point description:

The tool was EORTC QLQ-C30 questionnaire (C29+C30) version 3.0. (19). The recorded answers were transformed into dimensions ranged 0-100 according to the EORTC scoring instructions.

End point type	Secondary

End point timeframe:

Global quality of life was assessed before start of treatment, at every response evaluation, and at the end of treatment.

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: 0-100				
number (not applicable)	17			

Attachments (see zip file)	Quality of life Eudract..pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Toxicities were recorded at baseline, before every cycle and 30 days after the first day in the last cycle

Adverse event reporting additional description:

Toxicities were graded using The National Cancer Institute's Common Toxicity Criteria (NCI-CTC) version 4.0, year 2010.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Toxicity

Reporting group description:

Toxicity collected at baseline, before every cycle and 30 days after the first day in the last cycle.

Total number of deaths are collected as number of deaths to date (23.10.20)

Serious adverse events	Toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 26 (84.62%)		
number of deaths (all causes)	26		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Angina			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 26 (15.38%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	5 / 26 (19.23%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Vomiting				
subjects affected / exposed	4 / 26 (15.38%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	3 / 26 (11.54%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pain in stomach				
subjects affected / exposed	4 / 26 (15.38%)			
occurrences causally related to treatment / all	2 / 7			
deaths causally related to treatment / all	0 / 0			
Diarrhea				
subjects affected / exposed	3 / 26 (11.54%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 26 (3.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	4 / 26 (15.38%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Cough				
subjects affected / exposed	1 / 26 (3.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysnoe				
subjects affected / exposed	2 / 26 (7.69%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			

Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever			
subjects affected / exposed	9 / 26 (34.62%)		
occurrences causally related to treatment / all	7 / 13		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	4 / 26 (15.38%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	2 / 26 (7.69%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Urine infektion			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Toxicity		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 26 (100.00%)		
Investigations			
Grade 3-4 toxicities	Additional description: Please see toxicity table under endpoints.		
subjects affected / exposed	26 / 26 (100.00%)		
occurrences (all)	26		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 April 2017	Initially, the study included two arms; one with cabazitaxel and the other with tocotrienol. At progression or unacceptable toxicity of either of the treatments, cross-over to the other arm was allowed, although the study was not designed to compare the two treatment arms. Tocotrienol failed to reach its primary endpoint and the arm was closed at the time of the interim analysis. The Danish Medicines Agency decided that a new protocol and patient-information were needed. The study continued with a new protokol version 2, date 27.04.2017

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 April 2017	See Amendment description	29 May 2017

Notes:

Limitations and caveats

None reported