Clinical trial results:
A randomized, open-label, parallel-group, multi-center Phase II clinical trial evaluating effect of addition of DCVAC/OvCa to standard chemotherapy in women with relapsed platinum resistant epithelial ovarian carcinoma

Summary

EudraCT number	2013-001325-24
Trial protocol	CZ DE PL
Global end of trial date	02 August 2016

Results information

Result version number	v1 (current)
This version publication date	17 August 2017
First version publication date	17 August 2017
Summary attachment (see zip file)	Public Disclosure Summary_SOV03_Version 1.0_26-Jul-2017 (Public Disclosure Summary_SOV03_Version 1.0_26-Jul-2017.pdf)

Trial information

Trial identification

Sponsor protocol code	SOV03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02107378
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	SOTIO a.s.
Sponsor organisation address	Jankovcova 1518/2, Prague, Czech Republic, 170 00
Public contact	Clinical Trial Sotio, SOTIO a.s., +420 224175111, clinicaltrial@sotio.com
Scientific contact	Clinical Trial Sotio, SOTIO a.s., +420 224175111, clinicaltrial@sotio.com

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	02 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 August 2016
Global end of trial reached?	Yes
Global end of trial date	02 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the effect of adding DCVAC/OvCa to standard of care chemotherapy on overall survival in women with ovarian cancer who experienced relapse ≤6 months after achieving complete remission following standard first line (platinum-based) chemotherapy or did not reach complete remission

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Czech Republic: 16
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	20
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screened: 33; Randomized: 25; Analyzed for efficacy: 21; Analyzed for safety: 22

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group A

Arm description:

DCVAC/OvCa in parallel with standard of care chemotherapy (paclitaxel 80 mg/m2 intravenously [i.v.] on days 1, 8, 15, 22 of each 4-week cycle; or topotecan 4 mg/m2 i.v. on days 1, 8, 15 of each 4-week cycle; or liposomal doxorubicin 40 mg/m2 i.v. every 4 weeks)

Arm type	Experimental
Investigational medicinal product name	DCVAC/OvCa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of approximately 1×10e7 autologous dendritic cells

Arm title	Treatment group B

Arm description:

Standard of care chemotherapy only (paclitaxel 80 mg/m2 intravenously [i.v.] on days 1, 8, 15, 22 of each 4-week cycle; or topotecan 4 mg/m2 i.v. on days 1, 8, 15 of each 4-week cycle; or liposomal doxorubicin 40 mg/m2 i.v. every 4 weeks)

Arm type	Control

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Treatment group A	Treatment group B
Started	13	12
Completed	2	3
Not completed	11	9
Adverse event, serious fatal	3	2
Patient’s decision	1	3
Physician decision	1	2

Disease progression	3	2
DCVAC/OvCa manufacturing failure	2	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	25	25	
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)	20	20	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	25	25	
Male	0	0	

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomized patients regardless of whether they received treatment or not; patients randomized to treatment group A and who failed to receive at least 1 dose of DCVAC/OvCa were planned in the Protocol to be replaced and excluded from the ITT population. However, the sponsor decided to terminate the enrollment into this trial prematurely due to slow recruitment, and no patient was replaced.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

All randomized patients who received at least 3 cycles of standard of care chemotherapy and, for treatment group A, 8 doses of DCVAC/OvCa, did not violate any inclusion criteria, and did not have any major protocol violation. Before database lock, all protocol deviations were reviewed, and for each patient it was determined whether she belonged to the PP population or not. However, this population was not used in any analysis due to the low number of patients.

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who received at least 1 dose of standard of care chemotherapy or DCVAC/OvCa.

Reporting group values	ITT	PP	Safety
Number of subjects	21	7	22
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)	18		
From 65-84 years	3		
85 years and over	0		
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Treatment group A
Reporting group description:	
DCVAC/OvCa in parallel with standard of care chemotherapy (paclitaxel 80 mg/m2 intravenously [i.v.] on days 1, 8, 15, 22 of each 4-week cycle; or topotecan 4 mg/m2 i.v. on days 1, 8, 15 of each 4-week cycle; or liposomal doxorubicin 40 mg/m2 i.v. every 4 weeks)	
Reporting group title	Treatment group B
Reporting group description:	
Standard of care chemotherapy only (paclitaxel 80 mg/m2 intravenously [i.v.] on days 1, 8, 15, 22 of each 4-week cycle; or topotecan 4 mg/m2 i.v. on days 1, 8, 15 of each 4-week cycle; or liposomal doxorubicin 40 mg/m2 i.v. every 4 weeks)	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients regardless of whether they received treatment or not; patients randomized to treatment group A and who failed to receive at least 1 dose of DCVAC/OvCa were planned in the Protocol to be replaced and excluded from the ITT population. However, the sponsor decided to terminate the enrollment into this trial prematurely due to slow recruitment, and no patient was replaced.	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description:	
All randomized patients who received at least 3 cycles of standard of care chemotherapy and, for treatment group A, 8 doses of DCVAC/OvCa, did not violate any inclusion criteria, and did not have any major protocol violation. Before database lock, all protocol deviations were reviewed, and for each patient it was determined whether she belonged to the PP population or not. However, this population was not used in any analysis due to the low number of patients.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least 1 dose of standard of care chemotherapy or DCVAC/OvCa.	

Primary: Overall survival

End point title	Overall survival
End point description:	
Defined as the time from randomization until death due to any cause, ITT population	
End point type	Primary
End point timeframe:	
Until the end of the study	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: days				
median (inter-quartile range (Q1-Q3))	206 (180 to 1000000)	1000000 (100 to 1000000)		

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description: 1000000 means "not reached"	
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7208
Method	Logrank

Secondary: Progression-free survival

End point title	Progression-free survival
End point description: Measured by modifications to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1; defined as the time from randomization to tumor progression or death from any cause, ITT population	
End point type	Secondary
End point timeframe: Until the end of the study	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: days				
median (inter-quartile range (Q1-Q3))	52 (50 to 162)	100 (54 to 489)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.225
Method	Logrank

Secondary: Objective response rate

End point title	Objective response rate
End point description:	
Complete response and partial response, ITT population	
End point type	Secondary
End point timeframe:	
Until the end of the study	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: Not applicable				
number (confidence interval 95%)	0 (0 to 0.336)	0.167 (0.021 to 0.484)		

Statistical analyses

No statistical analyses for this end point

Secondary: Biological progression-free interval

End point title	Biological progression-free interval
End point description:	
Defined by increasing CA 125 levels according to Gynecologic Cancer Intergroup, ITT population	
End point type	Secondary
End point timeframe:	
Until the end of the study	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: Days				
median (inter-quartile range (Q1-Q3))	52 (50 to 162)	100 (54 to 489)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1278
Method	Logrank

Secondary: Immunological response

End point title	Immunological response

End point description:

Immunological response was not analyzed as a significant proportion of patients did not return for a sufficient number of visits.

End point type	Secondary

End point timeframe:

Until the end of the study

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: Not applicable				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Evaluation of quality of life using the standardized Functional Assessment of Cancer Therapy–Ovarian questionnaire

End point title	Evaluation of quality of life using the standardized Functional Assessment of Cancer Therapy–Ovarian questionnaire

End point description:

Functional Assessment of Cancer Therapy–Ovarian questionnaire scores showed that the treatment groups were similar in relation to quality of life.

End point type	Other pre-specified

End point timeframe:
Until the end of the study

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: Not applicable				
number (not applicable)	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the study treatment start date/time to 30 days after the last dose of study treatment (DCVAC/OvCa or standard of care chemotherapy)

Adverse event reporting additional description:

Adverse events were reported until 30 days after the last administration of DCVAC/OvCa (treatment group A) and until 30 days after the last dose of standard of care chemotherapy (treatment group B). Therefore, the reporting period differed significantly between the treatment groups (median duration 162 days in group A and 88.5 days in group B).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Treatment group A
Reporting group description: -	
Reporting group title	Treatment group B

Reporting group description: -

Serious adverse events	Treatment group A	Treatment group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 12 (66.67%)	3 / 10 (30.00%)	
number of deaths (all causes)	6	4	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancytopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Ascites			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment group A	Treatment group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)	9 / 10 (90.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Neuropathy peripheral			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
General physical health deterioration			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Asthenia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Leukopenia			

subjects affected / exposed	5 / 12 (41.67%)	2 / 10 (20.00%)	
occurrences (all)	5	2	
Anaemia			
subjects affected / exposed	5 / 12 (41.67%)	1 / 10 (10.00%)	
occurrences (all)	5	1	
Neutropenia			
subjects affected / exposed	5 / 12 (41.67%)	1 / 10 (10.00%)	
occurrences (all)	5	1	
Thrombocytopenia			
subjects affected / exposed	5 / 12 (41.67%)	0 / 10 (0.00%)	
occurrences (all)	5	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 12 (25.00%)	2 / 10 (20.00%)	
occurrences (all)	3	2	
Diarrhoea			
subjects affected / exposed	3 / 12 (25.00%)	2 / 10 (20.00%)	
occurrences (all)	3	2	
Ascites			
subjects affected / exposed	3 / 12 (25.00%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Intestinal obstruction			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Ileus			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Subileus			

subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	
occurrences (all)	3	1	
Hyperuricaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 August 2013	Specification of application sites (inguinal and axillary areas) for DCVAC/OvCa; specification of standard of care toxicity management based on institutional standards or applicable oncology guidelines; specification of pre treatment assessment of infection markers, if required by local/national regulations; correction of scheduling of the leukapheresis procedure and prolongation of the time frame for the transport of the cells harvested during the leukapheresis procedure to the processing facility; specification of time points of the follow up clinic visits and CA125 assessments.
21 November 2013	Specification of methods of contraception (exclusion criterion 13); added the justification of the applied DCVAC/OvCa dose; added the definition of slow progressive disease; added information about continuation of DCVAC/OvCa administration after disease progression; specification that not only the medications must be recorded, but the doses taken/administered as well; added information regarding the use of historical heart and lung X ray scans obtained prior to study entry; specification of exclusion criterion 6 (previous or concurrent radiotherapy to the abdomen and pelvis).
11 March 2014	Historical heart and lung X ray scans up to 4 weeks before screening are acceptable; change in the definition of secondary endpoints; specification of the follow up period including definition of the EoT visit, efficacy follow up and survival follow up; specification of the methods of contraception (exclusion criterion 13); changed the AE reporting period; definition and collection of SADRs; added determination of the sample size; added specification for patient replacement.
20 May 2014	Inclusion criteria 2 and 10, exclusion criteria 1 and 2; chest X-ray may be replaced by CT or thorax at investigators' decision; withdrawal of central reading for the evaluation of patient eligibility; specification that pregnant women must come for the EoT visit; during the efficacy follow up hematology, serum chemistry, and urinalysis tests were withdrawn; an independent blinded radiologist to evaluate sensitivity analysis of PFS and ORR.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported