



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 (carboplatin and gemcitabine) in women with relapsed platinum sensitive epithelial ovarian carcinoma

Summary

EudraCT number	2013-001323-38
Trial protocol	CZ DE PL
Global end of trial date	17 May 2018

Results information

Result version number	v1 (current)
This version publication date	06 June 2019
First version publication date	06 June 2019

Trial information

Trial identification

Sponsor protocol code	SOV02
-----------------------	-------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02107950
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	SOTIO a.s.
Sponsor organisation address	Jankovcova 1518/2, Prague, Czech Republic,
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	17 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2018
Global end of trial reached?	Yes
Global end of trial date	17 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

PRIMARY OBJECTIVE

The primary objective was to explore the effect of adding DCVAC/OvCa to chemotherapy on progression-free survival in women with ovarian cancer who experienced relapse >6 months after complete remission following platinum (Pt)-based first-line chemotherapy.

SECONDARY OBJECTIVES

- Overall survival
- Objective response rate
- Biological progression-free interval
- Immune response
- Safety
- Changes in quality of life

Protection of trial subjects:

Not applicable

Background therapy:

All patients were to receive chemotherapy with carboplatin and gemcitabine in 3-week cycles. On day 1 of each cycle, carboplatin area under the curve (AUC) 4-5 and gemcitabine 1000 mg/m² were to be administered, and on day 8 gemcitabine 1000 mg/m² was to be administered. A total of 6, 8, or 10 cycles of chemotherapy were to be completed as per investigators' decision. Chemotherapy was to be started within 7 days after leukapheresis for patients in treatment group A or within 2 weeks after randomization for patients in treatment group B.

Evidence for comparator: -

Actual start date of recruitment	04 November 2013
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: 50
Country: Number of subjects enrolled	Germany: 6
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	46
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Nine sites in the Czech Republic, 2 sites in Germany, and 4 sites in Poland screened at least 1 patient. Recruitment started on 04-Nov-2013 (first patient signed the informed consent form).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment group A

Arm description:

Patients in treatment group A received up to 10 subcutaneous doses of DCVAC/OvCa in addition to chemotherapy. The first 5 doses of DCVAC/OvCa were administered at 3-week intervals (with an acceptable window of ± 3 days), followed by dosing at 6-week intervals (with an acceptable window of ± 3 days). Each dose of DCVAC/OvCa was to be administered 4 ± 3 days before the nearest following dose of chemotherapy when given alongside the chemotherapy. The first dose of DCVAC/OvCa was administered after the second cycle of chemotherapy.

Arm type	Experimental
Investigational medicinal product name	DCVAC/OvCa
Investigational medicinal product code	Not applicable
Other name	Not applicable
Pharmaceutical forms	Dispersion for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of approximately 1×10^7 autologous dendritic cells

Arm title	Treatment group B
------------------	-------------------

Arm description:

No investigational medicinal product assigned in this arm

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Treatment group A	Treatment group B
Started	32	32
Completed	20	11
Not completed	12	21
Consent withdrawn by subject	2	8
Physician decision	1	1
Adverse event, non-fatal	-	1
Death	9	11

Baseline characteristics

Reporting groups

Reporting group title	Treatment group A
-----------------------	-------------------

Reporting group description:

Patients in treatment group A received up to 10 subcutaneous doses of DCVAC/OvCa in addition to chemotherapy. The first 5 doses of DCVAC/OvCa were administered at 3-week intervals (with an acceptable window of ± 3 days), followed by dosing at 6-week intervals (with an acceptable window of ± 3 days). Each dose of DCVAC/OvCa was to be administered 4 ± 3 days before the nearest following dose of chemotherapy when given alongside the chemotherapy. The first dose of DCVAC/OvCa was administered after the second cycle of chemotherapy.

Reporting group title	Treatment group B
-----------------------	-------------------

Reporting group description:

No investigational medicinal product assigned in this arm

Reporting group values	Treatment group A	Treatment group B	Total
Number of subjects	32	32	64
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	23	23	46
From 65-84 years	9	9	18
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	32	32	64
Male	0	0	0

End points

End points reporting groups

Reporting group title	Treatment group A
-----------------------	-------------------

Reporting group description:

Patients in treatment group A received up to 10 subcutaneous doses of DCVAC/OvCa in addition to chemotherapy. The first 5 doses of DCVAC/OvCa were administered at 3-week intervals (with an acceptable window of ± 3 days), followed by dosing at 6-week intervals (with an acceptable window of ± 3 days). Each dose of DCVAC/OvCa was to be administered 4 $\pm$ 3 days before the nearest following dose of chemotherapy when given alongside the chemotherapy. The first dose of DCVAC/OvCa was administered after the second cycle of chemotherapy.

Reporting group title	Treatment group B
-----------------------	-------------------

Reporting group description:

No investigational medicinal product assigned in this arm

Subject analysis set title	Intention-to-treat
----------------------------	--------------------

Subject analysis set type	Intention-to-treat
---------------------------	--------------------

Subject analysis set description:

The intention-to-treat (ITT) population consisted of all randomized patients regardless of whether they received treatment or not; however, patients randomized to treatment group A who failed to receive at least 1 dose of DCVAC/OvCa were to be replaced. More correctly, this is how a modified ITT population is defined; however, we referred to this population as to the ITT population.

Subject analysis set title	Per protocol
----------------------------	--------------

Subject analysis set type	Per protocol
---------------------------	--------------

Subject analysis set description:

The per protocol (PP) population consisted of all randomized patients who received at least 3 cycles of ChT and, for treatment group A, 8 doses of DCVAC/OvCa, did not violate any inclusion criteria, and did not have any major protocol deviations. Before database lock, all protocol deviations were reviewed, and for each patient it was determined whether he belonged to the PP population or not.

Primary: Progression-free survival, ITT population

End point title	Progression-free survival, ITT population
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

From randomization until the cut-off date of 21-Nov-2016

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: day				
median (inter-quartile range (Q1-Q3))	344.5 (286.0 to 455.5)	290.0 (233.0 to 399.0)		

Statistical analyses

Statistical analysis title	Primary analysis
----------------------------	------------------

Comparison groups	Treatment group A v Treatment group B
-------------------	---------------------------------------

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2736
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.28

Secondary: Progression-free survival, PP population

End point title	Progression-free survival, PP population
End point description:	
End point type	Secondary
End point timeframe:	
From randomization until the cut-off date of 21-Nov-2016	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: day				
median (inter-quartile range (Q1-Q3))	345.0 (290.0 to 456.0)	290.0 (233.0 to 399.0)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2224
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.24

Secondary: Overall survival as of the cut-off date, ITT population

End point title	Overall survival as of the cut-off date, ITT population
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization until the cut-off date of 21-Nov-2016

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: day				
median (inter-quartile range (Q1-Q3))	724.0 (675.0 to 778.0)	653.0 (514.0 to 1000000)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3028
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.54

Secondary: Overall survival as of the cut-off date, PP population

End point title	Overall survival as of the cut-off date, PP population
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization until the cut-off date of 21-Nov-2016

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: day				
median (inter-quartile range (Q1-Q3))	724.0 (675.0 to 778.0)	653.0 (514.0 to 1000000)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3028
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.54

Secondary: Overall survival at the end of the study, ITT population

End point title	Overall survival at the end of the study, ITT population
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization until the end of the study on 17-May-2018

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: day				
median (inter-quartile range (Q1-Q3))	1081.0 (724.0 to 1000000)	674.0 (514.0 to 951.0)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0032
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.74

Secondary: Overall survival at the end of the study, PP population

End point title	Overall survival at the end of the study, PP population
End point description:	
End point type	Secondary
End point timeframe:	
From randomization until the end of the study on 17-May-2018	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: day				
median (inter-quartile range (Q1-Q3))	1081.0 (724.0 to 1000000)	674.0 (514.0 to 951.0)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0032
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.74

Secondary: Objective response rate, ITT population

End point title	Objective response rate, ITT population
End point description:	
End point type	Secondary
End point timeframe:	
From randomization until the cut-off date of 21-Nov-2016	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: Not applicable				
number (confidence interval 95%)	0.875 (0.71 to 0.965)	0.625 (0.437 to 0.789)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate, PP population

End point title	Objective response rate, PP population
End point description:	
End point type	Secondary
End point timeframe:	
From randomization until the cut-off date of 21-Nov-2016	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Not applicable				
number (confidence interval 95%)	0.871 (0.702 to 0.964)	0.741 (0.537 to 0.889)		

Statistical analyses

No statistical analyses for this end point

Secondary: Biological progression-free interval, ITT population

End point title	Biological progression-free interval, ITT population
End point description:	
End point type	Secondary
End point timeframe:	
From randomization until the cut-off date of 21-Nov-2016	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: day				
median (inter-quartile range (Q1-Q3))	314.0 (286.0 to 411.5)	307.0 (230.0 to 398.0)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4777
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.43

Secondary: Biological progression-free interval, PP population

End point title	Biological progression-free interval, PP population
End point description:	
End point type	Secondary
End point timeframe:	
From randomization until the cut-off date of 21-Nov-2016	

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: day				
median (inter-quartile range (Q1-Q3))	319.0 (290.0 to 412.0)	307.0 (230.0 to 398.0)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Treatment group A v Treatment group B
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4062
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.39

Secondary: Immune response

End point title	Immune response
-----------------	-----------------

End point description:

The relationship between i) baseline levels of antibodies and T lymphocytes specific to NY-ESO-1 and MAGE-A1 and ii) the clinical endpoints progression-free survival and overall survival was explored by using a Cox proportional hazard regression model. This analysis did not indicate any statistically significant link between baseline levels of the immune parameters and the clinical endpoints.

The relationship between the levels of antibodies and T lymphocytes specific to NY-ESO-1 and MAGE-A1 after DCVAC/OvCa administration and the clinical endpoints progression-free survival and overall survival was explored by a case-by-case review of patients' data. A correlation between the immune response after DCVAC/OvCa administration and the clinical endpoints was observed in 2 patients.

End point type	Secondary
----------------	-----------

End point timeframe:

From randomization until the cut-off date of 21-Nov-2016

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: Not applicable	32	32		

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:

No signal was detected in terms of decrease in quality of life.

End point type	Other pre-specified
----------------	---------------------

End point timeframe:

From randomization until the cut-off date of 21-Nov-2016

End point values	Treatment group A	Treatment group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: Not applicable	32	32		

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 chemotherapy). Only 1 occurrence per patient per System Organ Class and Preferred Term is counted. PD-related AEs were not reportable per protocol.

Adverse event reporting additional description:

AEs were reported until 30 days after the last administration of DCVAC/OvCa (treatment group A) and until 30 days after the last dose of chemotherapy (treatment group B). Therefore, the reporting period differed significantly between the treatment groups (median duration 360 days in treatment group A and 150 days in treatment 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	20 / 37 (54.05%)	20 / 31 (64.52%)	
number of deaths (all causes)	11	11	
number of deaths resulting from adverse events	2	0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Explorative laparotomy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anaphylactic transfusion reaction			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular arrhythmia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	10 / 37 (27.03%)	13 / 31 (41.94%)	
occurrences causally related to treatment / all	0 / 10	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	6 / 37 (16.22%)	4 / 31 (12.90%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 37 (5.41%)	3 / 31 (9.68%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 37 (2.70%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumoperitoneum			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Toxic erythema of chemotherapy			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (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	2 / 37 (5.41%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Device related infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (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			
Cachexia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
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	36 / 37 (97.30%)	31 / 31 (100.00%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	2 / 37 (5.41%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Hypertension			
subjects affected / exposed	1 / 37 (2.70%)	3 / 31 (9.68%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 37 (27.03%)	4 / 31 (12.90%)	
occurrences (all)	10	4	
Asthenia			
subjects affected / exposed	3 / 37 (8.11%)	1 / 31 (3.23%)	
occurrences (all)	3	1	
Oedema peripheral			
subjects affected / exposed	2 / 37 (5.41%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	8 / 37 (21.62%)	5 / 31 (16.13%)	
occurrences (all)	8	5	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 37 (10.81%)	2 / 31 (6.45%)	
occurrences (all)	4	2	
Cough			
subjects affected / exposed	2 / 37 (5.41%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Dyspnoea exertional			
subjects affected / exposed	2 / 37 (5.41%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 31 (0.00%) 0	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 31 (3.23%) 1	
Platelet count decreased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 31 (3.23%) 1	
Weight decreased subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 31 (6.45%) 2	
Injury, poisoning and procedural complications Procedural nausea subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 31 (6.45%) 2	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	1 / 31 (3.23%) 1	
Polyneuropathy subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 31 (0.00%) 0	
Paraesthesia subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 31 (6.45%) 2	
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all)	21 / 37 (56.76%) 21	21 / 31 (67.74%) 21	
Anaemia subjects affected / exposed occurrences (all)	23 / 37 (62.16%) 23	20 / 31 (64.52%) 20	
Neutropenia			

subjects affected / exposed occurrences (all)	22 / 37 (59.46%) 22	21 / 31 (67.74%) 21	
Leukopenia subjects affected / exposed occurrences (all)	17 / 37 (45.95%) 17	9 / 31 (29.03%) 9	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	9 / 37 (24.32%) 9	7 / 31 (22.58%) 7	
Vomiting subjects affected / exposed occurrences (all)	7 / 37 (18.92%) 7	5 / 31 (16.13%) 5	
Diarrhoea subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 5	5 / 31 (16.13%) 5	
Abdominal pain subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	3 / 31 (9.68%) 3	
Constipation subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	5 / 31 (16.13%) 5	
Abdominal discomfort subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 31 (0.00%) 0	
Hepatobiliary disorders			
Liver disorder subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 31 (6.45%) 2	
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 31 (3.23%) 1	
Pruritus subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 31 (3.23%) 1	
Rash			

subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 31 (3.23%) 1	
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 31 (6.45%) 2	
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	2 / 31 (6.45%) 2	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	1 / 31 (3.23%) 1	
Pain in extremity subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	1 / 31 (3.23%) 1	
Back pain subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	1 / 31 (3.23%) 1	
Bone pain subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	0 / 31 (0.00%) 0	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	1 / 31 (3.23%) 1	
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	3 / 31 (9.68%) 3	
Viral infection subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	2 / 31 (6.45%) 2	
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	3 / 31 (9.68%) 3	

Infection			
subjects affected / exposed	1 / 37 (2.70%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Device related infection			
subjects affected / exposed	2 / 37 (5.41%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Oral herpes			
subjects affected / exposed	2 / 37 (5.41%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
Cystitis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	3 / 37 (8.11%)	4 / 31 (12.90%)	
occurrences (all)	3	4	
Decreased appetite			
subjects affected / exposed	2 / 37 (5.41%)	3 / 31 (9.68%)	
occurrences (all)	2	3	
Iron deficiency			
subjects affected / exposed	2 / 37 (5.41%)	1 / 31 (3.23%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 August 2013	Specification of the application site (groin and axillary areas) for DCVAC/OvCa; specification of ChT toxicity management based on institutional standards or applicable national/European oncology guidelines; specification of pretreatment assessment of infection markers, if required by local/national regulations; correction of scheduling 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 assessment.
21 November 2013	Specification of methods of contraception (exclusion criterion 13); added justification of the DCVAC/OvCa dose; added 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 using a historical heart and lung X ray scan obtained prior to study entry; specification of the exclusion criterion 6 (previous or concurrent radiotherapy to the abdomen and pelvis).
24 February 2014	Prolongation of screening period from originally up to 2 weeks to up to 4 weeks; specification of the follow-up period including definition of the EoT visit, efficacy follow-up, and survival follow up; specification of methods of contraception (exclusion criterion 13); change of inclusion criterion 3 (radiologically confirmed relapse after >6 months of remission (Pt-sensitive patients) to be found instead of originally up to 2 to up to 4 weeks prior to study entry); changed the AE reporting period; definition and collection of SADRs; added determination of the sample size; added specification for patients' replacement.
20 May 2014	Change in randomization (to be performed within 4 weeks after screening instead of 2 weeks after screening); change in inclusion criteria 2 and 10 and in exclusion criteria 1 and 2; chest X-ray may be replaced by CT of thorax at the investigator's decision; central reading no longer needed for evaluation of a patient's eligibility; specification that pregnant women must pass the EoT visit; correction in follow-up procedures in the Schedule of assessments; an independent blinded radiologist to evaluate CT/MRI scans for sensitivity analyses of PFS and ORR.
02 August 2016	Prolongation of the overall study duration by approximately 2 years as caused by extension of survival follow-up; the study is to be terminated after a sufficient number of events have been observed to evaluate mature OS. The main goal is that at least 50% of the total evaluable patients should have had a survival event. However, longer survival follow-up can be decided if deemed medically/statistically appropriate at the time of reaching the median survival (for the total group of patients in the study, i.e., without any separate study arm analysis). The item will be discussed with the trial SC (main investigators from the clinical trials SOV01, SOV02, SOV03, and a representative for the Polish sites) and the trial DMC for their recommendation to the sponsor regarding the length of the survival follow-up. Change in the frequency of telephone contacts during the survival follow-up period from 12 weeks to 6 months. Central reading of CT/MRI scans is to be considered only in case of a positive outcome of the analyses of the local evaluations or in case of a deemed need for health authority interactions. Addition of information on pharmacogenomics studies on research samples, which is relevant only for the Czech Republic (for operational reasons). (Pharmacogenomics research was approved as an addendum to the Protocol, version 4.1, in the Czech Republic. The sponsor added the already approved wording to the relevant part of the Protocol).

Notes:

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.

None reported

Notes: