Clinical trial results:
An open-label, single-group, multicenter phase II clinical trial evaluating the effect of maintenance DCVAC/OvCa after standard of care therapy in women with first relapse of platinum-sensitive epithelial ovarian carcinoma

Summary

EudraCT number	2017-002196-26
Trial protocol	CZ
Global end of trial date	25 February 2021

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	SOV06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03657966
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	SOTIO a.s.
Sponsor organisation address	Jankovcova 1518/2, Prague, Czechia, 17000
Public contact	Clinical Trial SOTIO, SOTIO a.s., clinicaltrial@sotio.com
Scientific contact	Clinical Trial SOTIO, SOTIO a.s., 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	22 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 February 2021
Global end of trial reached?	Yes
Global end of trial date	25 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

PRIMARY:
To explore if there was any added efficacy considering time to progression (by mRECIST version 1.1) or death (PFS) by adding DCVAC/OvCa as maintenance treatment after SoC with carboplatin/gemcitabine or carboplatin/paclitaxel in women with EOC who experienced relapse >6 months after complete remission following Pt-based first-line SoC. Efficacy was to be assessed vs. a historical control patient group treated in SOV02 trial with SoC alone in those who did not have progressive disease after 6 cycles of SoC.

SECONDARY:
•Overall survival versus a historical control patient group treated within the SOV02 trial (SoC alone and parallel DCVAC/OvCa treatment group)
•Biological progression-free interval versus a historical control patient group treated within the SOV02 trial (SoC alone and parallel DCVAC/OvCa treatment group)
•Best objective response (ORR)
•CA 125 response
•Time to response (objective response and CA 125 response)
•Immunological response
•Safety

Protection of trial subjects:

Not applicable.

Background therapy:

All patients were to receive standard of care chemotherapy.

For treatment with carboplatin/gemcitabine regimen, patients were to receive 1000 mg/m2 of gemcitabine as a 30-minute intravenous infusion on days 1 and 8 of 3-week cycles (with an acceptable window of ±3 days). Carboplatin (area under the curve [AUC] 4 mg/mL/min) was to be administered as an intravenous infusion (15 to 60 minutes) on day 1 of 3-week cycles (with an acceptable window of ±3 days).

For treatment with carboplatin/paclitaxel regime, 175 mg/m2 of paclitaxel was to be administered intravenously in a 3-hour infusion on day 1 of 3 week cycles (with an acceptable window of ±3 days). Carboplatin (AUC 5 mg/mL/min) was to be administered intravenously as a short-term infusion (15 to 60 minutes) on day 1 of 3 week cycles (with an acceptable window of ±3 days) as a short-term infusion (15 to 60 minutes).

A total of 6, 8, or 10 cycles of SoC chemotherapy were to be completed as per investigators' decision.

Evidence for comparator: -

Actual start date of recruitment	23 November 2017
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	Czechia: 2033
Worldwide total number of subjects	2033
EEA total number of subjects	2033

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)	1016
From 65 to 84 years	1017
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

NOTE: To allow input of results of comparison with historical control groups from trial SOV02, the number of patients that started and completed trial SOV06 has been artificially increased by 2000: +1000 for age group 18-64 years and +1000 for age group 65 to 84 years.

Pre-assignment

Screening details:

5 sites screened at least 1 patient. Recruitment started on 23-Nov-2017 (first patient signed the informed consent form).

Period 1

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

Arms

Arm title	Sequential DCVAC/OvCa

Arm description:

DCVAC/OvCa (approximately 1×107 autologous DCs) was to be administered at each dosing time to the patients subcutaneously. The first dose was to be administered 15 to 21 days after the last dose of SoC therapy. The first five doses of DCVAC/OvCa were to be given in 3-week intervals (with an acceptable window of ±3 days), followed by dosing at 6 week intervals (with an acceptable window of ±3 days) for a total of 15 doses.

NOTE: To allow input of results of comparison with historical control groups from trial SOV02, the number of patients that started and completed trial SOV06 has been artificially increased by 2000: +1000 for age group 18-64 years and +1000 for age group 65 to 84 years.

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:

An aliquot of approximately 1×10e7 activated autologous DCs (DCVAC/OvCa) will be thawed, re-suspended in 0.9% pre-cooled saline solution to a total volume of 5 mL, and divided in two 2.5 mL injections. The two injections will be administered subcutaneously in the axillary and the opposite inguinal lymph node areas.

Number of subjects in period 1	Sequential DCVAC/OvCa
Started	2033
Completed	2015
Not completed	18
Consent withdrawn by subject	2
Death	15
DCVAC/OvCa manufacturing failure	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)
Reporting group description:	
NOTE: To allow input of results of comparison with historical control groups from trial SOV02, the number of patients that started and completed trial SOV06 has been artificially increased by 2000: +1000 for age group 18-64 years and +1000 for age group 65 to 84 years.	

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	2033	2033	
Age categorical			
NOTE: To allow input of results of comparison with historical control groups from trial SOV02, the number of patients that started and completed trial SOV06 has been artificially increased by 2000: +1000 for age group 18-64 years and +1000 for age group 65 to 84 years.			
Units: Subjects			
Adults (18-64 years)	1016	1016	
From 65-84 years	1017	1017	
Gender categorical			
NOTE: To allow input of results of comparison with historical control groups from trial SOV02, the number of patients that started and completed trial SOV06 has been artificially increased by 2000: +1000 for age group 18-64 years and +1000 for age group 65 to 84 years.			
Units: Subjects			
Female	2033	2033	

End points

End points reporting groups

Reporting group title	Sequential DCVAC/OvCa

Reporting group description:

DCVAC/OvCa (approximately 1×107 autologous DCs) was to be administered at each dosing time to the patients subcutaneously. The first dose was to be administered 15 to 21 days after the last dose of SoC therapy. The first five doses of DCVAC/OvCa were to be given in 3-week intervals (with an acceptable window of ±3 days), followed by dosing at 6 week intervals (with an acceptable window of ±3 days) for a total of 15 doses.

NOTE: To allow input of results of comparison with historical control groups from trial SOV02, the number of patients that started and completed trial SOV06 has been artificially increased by 2000: +1000 for age group 18-64 years and +1000 for age group 65 to 84 years.

Subject analysis set title	SOV02 Parallel DCVAC/OvCa (mITT population)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

A historical control patient group treated within the SOV02 trial with SoC chemotherapy and parallel DCVAC/OvCa.

Subject analysis set title	SOV02 SoC (mITT population)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

A historical control patient group treated within the SOV02 trial with SoC chemotherapy only.

Primary: PFS measured according to the modified RECIST 1.1 (mITT population)

End point title	PFS measured according to the modified RECIST 1.1 (mITT population)

End point description:

End point type	Primary

End point timeframe:

From eligibility verification to the date of an event defined as the first radiological progression or death due to any cause, whichever occurs first.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	26	20	
Units: month				
median (confidence interval 95%)	9.7 (7.7 to 13.1)	12.4 (10.1 to 14.9)	11.1 (7.7 to 13.1)	

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.3494
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.57

Notes:

[1] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.9361
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.9

Notes:

[2] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Primary: PFS measured according to the modified RECIST 1.1 (PP population)

End point title	PFS measured according to the modified RECIST 1.1 (PP population)

End point description:

End point type	Primary

End point timeframe:

From eligibility verification to the date of an event defined as the first radiological progression or death due to any cause, whichever occurs first.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25	20	
Units: month				
median (confidence interval 95%)	9.4 (7.7 to 13.8)	13.4 (10.2 to 14.9)	11.1 (7.7 to 13.1)	

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.3138
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.76

Notes:

[3] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.9523
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.96

Notes:

[4] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Primary: PFS measured according to the modified RECIST 1.1 (ITT population)

End point title	PFS measured according to the modified RECIST 1.1 (ITT population)

End point description:

End point type	Primary

End point timeframe:

From eligibility verification to the date of an event defined as the first radiological progression or death due to any cause, whichever occurs first.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	33	39	32	
Units: month				
median (confidence interval 95%)	9.7 (7.7 to 12.6)	11.3 (9.5 to 13.9)	10.6 (7.7 to 12.7)	

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.5723
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.17

Notes:

[5] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.9347
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.81

Notes:

[6] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Secondary: Overall survival (mITT population)

End point title	Overall survival (mITT population)

End point description:

End point type	Secondary

End point timeframe:

From eligibility verification till death due to any cause.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	30[7]	26[8]	20	
Units: month				
median (confidence interval 95%)	30 (21.3 to 1000)	35.5 (25.6 to 1000)	22.2 (17.2 to 36.1)	

Notes:

[7] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

[8] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	= 0.432
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	2.88
Variability estimate	Standard deviation

Notes:

[9] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.1009
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	1.14

Notes:

[10] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Secondary: Overall survival (PP population)

End point title	Overall survival (PP population)

End point description:

End point type	Secondary

End point timeframe:

From eligibility verification till death due to any cause.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	25[11]	25[12]	20	
Units: month				
median (confidence interval 95%)	30.4 (23.6 to 1000)	35.5 (25.6 to 1000)	22.2 (17.2 to 36.1)	

Notes:

[11] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

[12] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	= 0.6596
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	2.67

Notes:

[13] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.0563
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	1.02
Variability estimate	Standard deviation

Notes:

[14] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Secondary: Overall survival (ITT population)	
End point title	Overall survival (ITT population)

End point description:

End point type	Secondary

End point timeframe:

From eligibility verification till death due to any cause.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	33[15]	39	32	
Units: month				
median (confidence interval 95%)	30 (21.3 to 1000)	29.5 (23.1 to 45)	22.2 (17.2 to 32.5)	

Notes:

[15] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	= 0.9703
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.94

Notes:

[16] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.034
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.95

Notes:

[17] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Secondary: Biological progression-free interval (mITT population)

End point title	Biological progression-free interval (mITT population)

End point description:

End point type	Secondary

End point timeframe:

From the date of the eligibility verification till progression in CA 125 according to GCIG criteria.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	26[18]	20[19]	
Units: month				
median (confidence interval 95%)	9.9 (8.5 to 12.5)	13.4 (11.3 to 1000)	15.5 (9.8 to 1000)	

Notes:

[18] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

[19] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 0.009
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	5.85

Notes:

[20] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 0.0525
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	2.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	7.45

Notes:

[21] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

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 the date of the eligibility verification till progression in CA 125 according to GCIG criteria.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25[22]	20[23]	
Units: month				
median (confidence interval 95%)	10.7 (8.5 to 12.6)	13.4 (11.3 to 1000)	15.5 (9.8 to 1000)	

Notes:

[22] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

[23] - Value 1000 in CIs means that the CI could not be calculated, therefore it is not applicable.

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[24]
P-value	= 0.03
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	5.23

Notes:

[24] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other[25]
P-value	= 0.1125
Method	Adjusted Cox PH model
Parameter estimate	Hazard ratio (HR)
Point estimate	2.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	6.63

Notes:

[25] - Adjusted Cox PH model. Adjustment performed on age, log (baseline CA 125) and ECOG.

Secondary: Objective response rate (mITT population)

End point title	Objective response rate (mITT population)

End point description:

End point type	Secondary

End point timeframe:

From the start of SoC treatment until disease progression, death or end of trial treatment (SoC or DCVAC/OvCa, whichever occurred later) + 30 days, whichever occurred first.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	26	20	
Units: percent				
number (confidence interval 95%)	70 (53.6 to 86.4)	88.5 (76.2 to 100)	85 (69.4 to 100)	

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other[26]
P-value	= 0.0931
Method	Chi-squared
Parameter estimate	Difference
Point estimate	-18.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.9
upper limit	2

Notes:

[26] - Difference in proportions by a Chi-squared test.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[27]
P-value	= 0.2237
Method	Chi-squared
Parameter estimate	Difference
Point estimate	-15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.7
upper limit	7.7

Notes:

[27] - Difference in proportions by Chi-squared test.

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 the start of SoC treatment until disease progression, death or end of trial treatment (SoC or DCVAC/OvCa, whichever occurred later) + 30 days, whichever occurred first.

End point values	Sequential DCVAC/OvCa	SOV02 Parallel DCVAC/OvCa (mITT population)	SOV02 SoC (mITT population)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	25	25	20	
Units: percent				
number (confidence interval 95%)	76 (59.3 to 92.7)	88 (75.3 to 100)	85 (69.4 to 100)	

Statistical analyses

Statistical analysis title	Main analysis vs. parallel DCVAC/OvCa
Comparison groups	Sequential DCVAC/OvCa v SOV02 Parallel DCVAC/OvCa (mITT population)

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0.2695
Method	Chi-squared
Parameter estimate	Difference
Point estimate	-12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33
upper limit	9

Notes:

[28] - Difference in proportions by a Chi-squared test.

Statistical analysis title	Main analysis vs. SoC
Comparison groups	Sequential DCVAC/OvCa v SOV02 SoC (mITT population)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.4533
Method	Chi-squared
Parameter estimate	Difference
Point estimate	-9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.9
upper limit	13.9

Notes:

[29] - Difference in proportions by a Chi-squared test.

Secondary: Time to response according to modified RECIST 1.1 (mITT population)	
End point title	Time to response according to modified RECIST 1.1 (mITT population)

End point description:

End point type	Secondary

End point timeframe:

From eligibility verification until the first objective tumor response (CR or PR).

End point values	Sequential DCVAC/OvCa			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: month				
median (confidence interval 95%)	2.2 (2.1 to 2.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response according to modified RECIST 1.1 (PP population)

End point title	Time to response according to modified RECIST 1.1 (PP population)

End point description:

End point type	Secondary

End point timeframe:

From eligibility verification until the first objective tumor response (CR or PR).

End point values	Sequential DCVAC/OvCa			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: month				
median (confidence interval 95%)	2.2 (2.1 to 3.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients exposed to DCVAC/OvCa:
From the date of the patient's signing the ICF until 30 days after the final administration of DCVAC/OvCa (SAEs with a plausible causal relationship to DCVAC/OvCa must be reported until indefinitely).

Adverse event reporting additional description:

Patients not exposed to DCVAC/OvCa:
From ICF signature until:
•1 day after leukapheresis or DCVAC/OvCa manufacturing failure (before SoC therapy initiation)
•30 days after the last SoC therapy cycle
•following the patient's ICF withdrawal
Progression of underlying disease or AE related to progression does not need to be reported as SAE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Sequential DCVAC/OvCa

Reporting group description:

DCVAC/OvCa (approximately 1×10e7 autologous DCs) was to be administered at each dosing time to the patients subcutaneously. The first dose was to be administered 15 to 21 days after the last dose of SoC therapy. The first five doses of DCVAC/OvCa were to be given in 3-week intervals (with an acceptable window of ±3 days), followed by dosing at 6 week intervals (with an acceptable window of ±3 days) for a total of 15 doses.

NOTE: There were 3 TEAEs with a fatal outcome associated with the progression of underlying disease. Per protocol, progression of the underlying disease or an AE unequivocally (without doubt) related to the progression of the underlying disease, regardless of its outcome or seriousness criteria, does not need to be reported as an SAE. However, there was 1 fatal SUSAR reported (PT: Myelodysplastic syndrome) in a patient in the follow-up period as defined by the protocol. The SUSAR is recorded in the Safety Database.

Serious adverse events	Sequential DCVAC/OvCa		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 32 (34.38%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Haematemesis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related sepsis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Sequential DCVAC/OvCa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 32 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 21		
General physical health deterioration subjects affected / exposed occurrences (all)	6 / 32 (18.75%) 6		
Pain subjects affected / exposed occurrences (all)	3 / 32 (9.38%) 10		
Pyrexia subjects affected / exposed occurrences (all)	3 / 32 (9.38%) 3		
Oedema peripheral subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	4 / 32 (12.50%) 4		
Respiratory, thoracic and mediastinal disorders Pleural effusion subjects affected / exposed occurrences (all)	5 / 32 (15.63%) 6		
Cough subjects affected / exposed occurrences (all)	3 / 32 (9.38%) 4		
Dyspnoea subjects affected / exposed occurrences (all)	3 / 32 (9.38%) 3		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	4 / 32 (12.50%) 4		
Depression subjects affected / exposed occurrences (all)	4 / 32 (12.50%) 4		
Investigations			

Weight decreased subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Polyneuropathy subjects affected / exposed occurrences (all)	 4 / 32 (12.50%) 4 3 / 32 (9.38%) 6 2 / 32 (6.25%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Leukocytosis subjects affected / exposed occurrences (all)	 21 / 32 (65.63%) 32 17 / 32 (53.13%) 30 10 / 32 (31.25%) 15 3 / 32 (9.38%) 3 2 / 32 (6.25%) 2		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 2 / 32 (6.25%) 2		
Eye disorders Photopsia subjects affected / exposed occurrences (all)	 2 / 32 (6.25%) 2		

Cataract			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	18 / 32 (56.25%)		
occurrences (all)	41		
Diarrhoea			
subjects affected / exposed	9 / 32 (28.13%)		
occurrences (all)	16		
Vomiting			
subjects affected / exposed	9 / 32 (28.13%)		
occurrences (all)	13		
Abdominal pain			
subjects affected / exposed	9 / 32 (28.13%)		
occurrences (all)	11		
Ascites			
subjects affected / exposed	8 / 32 (25.00%)		
occurrences (all)	9		
Abdominal pain upper			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	8		
Dyspepsia			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	6		
Constipation			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	6		
Asthenia			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	6		
Abdominal discomfort			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	6		
Stomatitis			

subjects affected / exposed occurrences (all) Mechanical ileus subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2 2 / 32 (6.25%) 2 2 / 32 (6.25%) 2 2 / 32 (6.25%) 2		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all)	 2 / 32 (6.25%) 7 2 / 32 (6.25%) 2 2 / 32 (6.25%) 2		
Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all) Dysuria subjects affected / exposed occurrences (all)	 2 / 32 (6.25%) 2 2 / 32 (6.25%) 2		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Back pain	 5 / 32 (15.63%) 8 3 / 32 (9.38%) 7		

subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Muscle spasms			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	8 / 32 (25.00%)		
occurrences (all)	14		
Upper respiratory tract infection			
subjects affected / exposed	7 / 32 (21.88%)		
occurrences (all)	8		
Nasopharyngitis			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Cystitis			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	7		
Oral herpes			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Bacteriuria			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Laryngitis			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Asymptomatic bacteriuria			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	9 / 32 (28.13%)		
occurrences (all)	21		
Hypomagnesaemia			

subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	6		
Decreased appetite			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2017	• Clarification in the statistical sections • ECOG performance status not to be measured during the survival follow-up period
18 December 2017	• The number of doses increased from up to 10 to up to 15 • Schedule of sample collection for exploratory immunological research changed to reflect the change in the number of DCVAC/OvCa doses administered per patient • Exact time points added for vital signs measured after the DCVAC/OvCa administration • Acceptable visit window added for SoC therapy and efficacy follow up period • Historical chest X ray and/or CT/MRI of the abdomen and pelvis up to 4 weeks are acceptable. • Collaboration with CEEGOG • Wording adjusted to reflect changes and to clarify meaning; minor corrections of grammar
21 May 2019	• Date of DCVAC/OvCa administration: tb calculated from the date of the previous DCVAC/OvCa administration • Addition of IDMC • All patients eligible at final eligibility assessment are tb followed for OS and further-line anticancer therapy • All time-to-event analyses are tb measured from eligibility verification • The control group from SOV02 trial is to include only patients who did not have PD after 6 cycles of SoC chemotherapy • Modification of the definition of ITT population, addition of mITT population, clarification of PP population • CA 125 levels are not tb considered in evaluation of non-target lesions • Response assessment is to take place after 6 cycles of SoC chemotherapy • Independent review of CT/MRI scans is to be considered in case of need for health authority interactions • CT/MRI does not take place during efficacy follow-up visits • Hematology, serum chemistry, and urinalysis tests performed at the trial site 1-3 days before the start of a treatment cycle are acceptable • Patients are to discontinue DCVAC/OvCa in case of a systemic allergic reaction to DCVAC/OvCa • The version of the MedDRA current at the time of database lock is to be used • Inclusion criterion 3: the relapse after >6 months of remission (Pt-sensitive cancer) should be radiologically confirmed up to 4 weeks prior to signing the ICF or during screening • Urine does not have to be tested only by dipstick • APTT is to be reported in seconds or ratio • Urea is to be tested and not both urea and blood urea nitrogen • CT/MRI scans are to be done at screening, every 8 weeks (± 3 days) after SoC therapy initiation, or every 8 weeks (± 3 days) from the previous CT/MRI, i.e., ideally till 104 weeks (± 3 days) after SoC therapy initiation • After confirmed disease progression after second-line SoC therapy, vascular endothelial GF inhibitors administered according to the SPC are allowed • Removal of obsolete information and changes in wording to improve readability

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.

To allow input of results of comparison with historical control groups from trial SOV02, the number of patients in trial SOV06 has been artificially increased by 2000: +1000 for age group 18-64 years and +1000 for age group 65-84 years.

Notes: