Public Disclosure Summary
Study SOV03

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NAME OF SPONSOR

SOTIO a.s., Jankovcova 1518/2, 170 00 Prague, Czech Republic

NAME OF FINISHED TEST PRODUCT

DCVAC/OvCa

NAME OF ACTIVE INGREDIENT

Autologous dendritic cells pulsed with killed ovarian cancer cells and matured by a Toll-like receptor 3 ligand

TITLE OF STUDY

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

STUDY CENTERS AND COUNTRIES

Twenty-two sites participated in the study, out of which 11 recruited at least 1 patient: 6 sites in the Czech Republic, 1 site in Germany, and 4 sites in Poland.

STUDY PERIOD

Study initiation date (first patient signed the Informed Consent Form): 16-Jan-2014

Study completion date: 02-Aug-2016

REPORTING PERIOD

From: 16-Jan-2014 (first patient signed the Informed Consent Form)

To: 02-Aug-2016 (study completion)

PHASE OF DEVELOPMENT

II

BACKGROUND AND RATIONALE

Surgical removal of the tumor and platinum (Pt)-taxane-based chemotherapy remains the core primary treatment for ovarian cancer. Despite good response rates to initial therapy, most women develop recurrent ovarian cancer. The 5-year survival rate is reported to span from 94% in women diagnosed at an early stage of the disease to only 17% in women diagnosed with advanced disease. Novel therapeutic approaches are therefore needed to enhance treatment outcomes.

One innovative treatment option available to test in the setting of recurrent ovarian cancer is immunotherapy administered as an add-on to the already existing standard of care chemotherapy (SoC). Cancer immunotherapy can employ various immune system components to combat the disease. In this study, autologous dendritic cells (DCs) were used. The test product DCVAC/OvCa is a patient-specific active cellular immunotherapy which uses autologous DCs activated by transient *ex vivo* exposure to killed ovarian cancer cells. We hypothesized that when the activated DCs are injected back into the patient with ovarian cancer, an immune response is established against the cancer that may inhibit disease progression and potentially improve overall survival (OS). It is assumed that a minimum of 8 doses of DCVAC/OvCa are needed to achieve a therapeutic effect.

To test this hypothesis, several clinical trials with DCVAC/OvCa in different settings were set up, including the current trial. Initially, the first-in-human investigator-initiated clinical trial with DCVAC/OvCa (EudraCT: 2010-021462-30) was conducted in the Czech Republic at the University Hospital Motol. It was a non-randomized, open-label, single-center, phase I clinical trial in women with Féderation Internationale de Gynécologie et d'Obstétrique (FIGO) stage III-IV ovarian cancer following primary cytoreduction surgery and at least 1 cycle of chemotherapy based on taxane and Pt derivative combination. Eight out of 10 planned women were enrolled in the trial; however, only 7 women were exposed to DCVAC/OvCa. An additional 3 women were treated on an individual basis outside of the clinical trial. A total of approximately 120 applications of DCVAC/OvCa were administered to these 10 women. In this study, DCVAC/OvCa had a favorable safety profile and induced immune response against relevant tumor antigens.

The clinical trial SOV03 was a randomized, open-label, parallel-group, multi-center phase II clinical trial to explore the effect on OS of adding DCVAC/OvCa to SoC with paclitaxel or topotecan or liposomal doxorubicin in women with ovarian cancer who experienced relapse ≤6 months after achieving complete remission following standard first-line (Pt-based) chemotherapy or who did not reach complete remission. Secondary objectives of the trial SOV03 included progression-free survival (PFS), objective response (OR) rate (ORR), biological progression-free interval (PFI_{BIO}), immunological response, safety, and changes in quality of life (QoL). The trial enrolled only 25 women from January 2014 until March 2015, and the sponsor decided to terminate the enrollment due to slow recruitment.

OBJECTIVES

Primary objective:

The primary objective was to explore the effect of adding DCVAC/OvCa to SoC on OS in women with ovarian cancer who experienced relapse ≤6 months after achieving complete remission following standard first-line (Pt-based) chemotherapy or who did not reach complete remission.

Secondary objectives:

- PFS
- ORR (complete response [CR] and partial response [PR])
- PFI_{BIO}

- Immunological response
- Safety
- Changes in QoL

ENDPOINTS

Primary endpoint:

- OS (until the End of Study [EoS]) defined as the time from randomization until death due to any cause

Secondary endpoints:

- PFS measured by modifications to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. PFS was defined as the time from randomization to tumor progression or death from any cause.
- ORR (CR and PR measured according to RECIST 1.1 criteria)
- PFI_{BIO} defined by increasing cancer antigen 125 (CA 125) levels (Gynecologic Cancer Intergroup [GCIG])
- Immunological response – detection of entire anti-tumor response

Exploratory endpoint:

- Evaluation of QoL using the standardized Functional Assessment of Cancer Therapy-Ovarian (FACT-O) questionnaire

Safety endpoints:

- Adverse events (AEs), including laboratory abnormalities

METHODOLOGY

This was a randomized, open-label, multicenter, parallel-group phase II study to explore the efficacy and safety of DCVAC/OvCa added to SoC in women with ovarian cancer demonstrating incomplete or short-lasting response to Pt-based first-line chemotherapy (Pt-resistant, partial responders, or Pt-refractory).

Patients were evaluated for eligibility during a screening period lasting up to 4 weeks and included in the study once the failure of first-line Pt-based chemotherapy was confirmed by computed tomography (CT)/magnetic resonance imaging (MRI) scan or by a finding described as "did not reach complete clinical remission"; progression could not have been confirmed by CA 125 measurements. Eligible patients were randomized to 2 groups at a ratio of 1:1 to receive immunotherapy in parallel with SoC (treatment group A) or SoC alone (treatment group B). The target was to randomize a total of 60 patients.

Patients in treatment group A were evaluated for feasibility of leukapheresis and were to undergo leukapheresis within 7 days after randomization. Patients in treatment group B did not undergo leukapheresis.

All patients were to receive SoC (paclitaxel 80 mg/m^2 intravenously [i.v.] on days 1, 8, 15, 22 of each 4-week cycle; or topotecan 4 mg/m^2 i.v. on days 1, 8, 15 of each 4-week cycle; or liposomal doxorubicin 40 mg/m^2 i.v. every 4 weeks) per investigators' choice starting 11±3 days after the leukapheresis procedure for patients in treatment group A and within 3 weeks after randomization for patients in treatment group B.

Patients in treatment group A were to receive up to 10 subcutaneous doses of DCVAC/OvCa in addition to SoC. The first dose of DCVAC/OvCa was administered after the first cycle of SoC. All subsequent doses of DCVAC/OvCa were to be given at 4-week intervals (±3 days). Where possible, DCVAC/OvCa was to be administered at least 7 days before the nearest following dose of SoC. If concurrent application of DCVAC/OvCa and SoC was unavoidable, DCVAC/OvCa was to be administered before SoC and related medications.

Patients randomized to treatment group B received SoC only; placebo was not used.

The treatment phase of the study ended with the End of Treatment (EoT) visit to be performed 30 days after the last dose of DCVAC/OvCa for patients in treatment group A and 30 days after the last dose of SoC for patients in treatment group B.

After the EoT visit, patients were to be followed for efficacy by clinical visits at 8-week intervals until 72 weeks after the initiation of SoC or until refusal or death. After the end of the efficacy follow-up, patients were to be followed up for survival by a phone call every 12 weeks (±1 week) until the EoS.

The EoS took place 72 weeks after the initiation of SoC of the last patient enrolled in the study.

This study was not blinded.

An independent Data Monitoring Committee and a Steering Committee were established before the randomization of the first patient.

NUMBER OF PATIENTS

Planned: 60

The trial enrolled only 25 women from January 2014 until March 2015, and the sponsor decided to terminate the enrollment due to slow recruitment.

Screened: 33

Randomized: 25

Analyzed for efficacy: 21

Analyzed for safety: 22

DIAGNOSIS AND CRITERIA FOR INCLUSION AND EXCLUSION

Diagnosis:

Women with ovarian cancer who experienced relapse ≤6 months after achieving complete remission following standard first-line (Pt-based) chemotherapy or who did not reach complete remission.

Inclusion criteria:

1. Female aged ≥18 years
2. Patients with histologically confirmed FIGO stage III and IV epithelial ovarian, primary peritoneal, or fallopian tube carcinoma (serous, endometrioid, or mucinous), who underwent initial surgery or interval debulking surgery but did not reach complete remission of more than 6 months after first-line Pt-based chemotherapy for one of the following reasons:
   - ~ Patients were Pt-refractory (no response)
   - ~ Complete remission was not reached (partial responders)
   - ~ Relapse within ≤6 months of remission (Pt-resistant)
3. Pt-based chemotherapy failure should have been confirmed by CT/MRI scan (Pt-resistant) or by a finding described as "did not reach complete clinical remission" (Pt-refractory or Pt-partial response). Patients were selected to receive second-line SoC.
4. Patients had to have at least one measureable target lesion as defined by RECIST 1.1 criteria.
5. Laboratory criteria (results had to be obtained <14 days before randomization, including results obtained before giving informed consent):
   - ~ White blood cells (WBC) >4000/mm^3 (4.0×10^9/L)
   - ~ Neutrophil count >1500/mm^3 (1.5×10^9/L)
   - ~ Hemoglobin (Hb) ≥10 g/dL (100 g/L)
   - ~ Platelet count ≥100,000/mm^3 (100×10^9/L)
   - ~ Total bilirubin within normal limits (benign hereditary hyperbilirubinemias, e.g., Gilbert's syndrome are permitted)
   - ~ Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <2× upper limit of normal (ULN), serum creatinine ≤2.0 mg/dL
   - ~ Blood urea nitrogen <2.0×ULN
6. Adequate coagulation parameters (results had to be obtained <14 days before randomization, including results obtained before giving informed consent):
   - ~ Activated partial thromboplastin time (APTT) ≤1.5×ULN and
   - ~ International normalized ratio (INR) ≤1.5
7. Life expectancy of at least 12 months based on investigators' judgment
8. Eastern Cooperative Oncology Group (ECOG) performance status 0-2
9. Signed informed consent including the patient's ability to comprehend its contents
10. Females of childbearing potential (assessed by the investigator) had to have a negative serum pregnancy test at screening (β human chorionic gonadotropin)

Exclusion criteria:

1. FIGO I, II epithelial ovarian cancer
2. FIGO III, IV clear cells epithelial ovarian cancer
3. Non-epithelial ovarian cancer
4. Borderline tumors (tumors of low malignant potential)
5. Prior or current systemic anti-cancer therapy for ovarian cancer (for example chemotherapy, monoclonal antibody therapy, tyrosine kinase inhibitor therapy (TKI), vascular endothelial growth factor [VEGF] therapy or hormonal therapy) except first line Pt based chemotherapy (with or without bevacizumab)
6. Previous or concurrent radiotherapy to the abdomen and pelvis
7. Malignancy other than epithelial ovarian cancer, except those that have been in complete remission for a minimum of 3 years, and except carcinoma *in situ* of the cervix or non-melanoma skin carcinomas
8. Patient co morbidities:
   - ~ Human immunodeficiency virus (HIV) positive, human T-lymphotropic virus (HTLV) positive
   - ~ Active hepatitis B (HBV), active hepatitis C (HCV), active syphilis
   - ~ Evidence of active bacterial, viral, or fungal infection requiring systemic treatment
   - ~ Clinically significant cardiovascular disease including:
     - Symptomatic congestive heart failure
     - Unstable angina pectoris
     - Serious cardiac arrhythmia requiring medication
     - Uncontrolled hypertension
     - Myocardial infarction or ventricular arrhythmia or stroke within a 6 month period before inclusion, ejection fraction <40% or serious cardiac conduction system disorders, if a pacemaker is not present
   - ~ Pericardial effusion of any National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI CTCAE) grade
   - ~ Peripheral neuropathy having a CTCAE Grade ≥2

- ~ Active autoimmune disease requiring treatment
- ~ History of severe forms of primary immune deficiencies
- ~ History or anaphylaxis or other serious reaction following vaccination
- ~ Uncontrolled co-morbidities including psychiatric or social conditions which, in the investigator's opinion, would prevent participation in the trial

9. Known hypersensitivity to any constituent of DCVAC/OvCa
10. Systemic immunosuppressive therapy for any reason
11. Refusal to sign the informed consent
12. Participation in a clinical trial using experimental therapy within the last 4 weeks before study entry; patients previously enrolled in the study SOV01 who did not receive treatment with DCVAC/OvCa could have been included in this study
13. Fertile woman of childbearing potential not willing to use a highly effective method of contraception or a combination of methods resulting into PEARL Index <1 (implants, injectables, combination of oral contraceptives with intrauterine devices or barrier method of contraception or spermicidal jelly, vasectomized / sterilized partner or sexual abstinence) for the study duration and at least 6 months afterwards
14. Pregnant or lactating women

TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION, BATCH NUMBER(S)

Test product:

DCVAC/OvCa, an active cellular immunotherapy product containing DCs activated by exposure to killed tumor cells of the ovarian cancer cell lines SK-OV-3 and OV-90 and matured by poly(I:C), a Toll-like receptor 3 ligand.

Dose and mode of administration:

An aliquot of 5 mL of cell suspension containing approximately 1×10^7 autologous DCs was divided into 2 injections (2.5 mL each) that were applied subcutaneously to the inguinal and axillary regions.

Batch number:

DCVAC/OvCa was prepared on an individual basis, each product with a unique batch number.

DURATION OF TREATMENT WITH TEST PRODUCT

Up to 10 doses of DCVAC/OvCa were administered during approximately 36 weeks to patients randomized to treatment group A.

CONTROL PRODUCT, DOSE AND MODE OF ADMINISTRATION, BATCH NUMBER(S)

NA

DURATION OF TREATMENT WITH CONTROL PRODUCT

NA

STATISTICAL METHODS

Randomized patients were allocated to trial populations for analysis purposes. The Intent-to-treat population (ITT) consisted of 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. The ITT population included 9 patients in treatment group A and 12 patients in treatment group B. The Per Protocol population (PP) included all randomized patients who received at least 3 cycles of SoC and, for treatment group A, 8 doses of DCVAC/OvCa, did not violate any inclusion criteria, and did not have any major protocol violation (2 patients in treatment group A and 5 patients in treatment group B). However, this population was not used in any analysis due to the low number of patients. The safety population consisted of all patients who received at least 1 dose of SoC or DCVAC/OvCa (12 patients in treatment group A and 10 patients in treatment group B).

Demographic and other baseline characteristics were summarized and presented by treatment group. Medical/surgical history was coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 19.1 to the preferred term (PT) and system organ class (SOC).

The primary endpoint was analyzed using the ITT population as follows. The number and percentage of patients achieving OS at the EoS were presented by treatment group. Kaplan-Meier estimates for median OS and the 25th and 75th quartiles were presented by treatment groups. A graphic presentation of the Kaplan-Meier estimates supplemented the tabular presentation. The Kaplan-Meier estimates for OS at the EoS were also presented by subgroups (different types of SoC). A log-rank test was used for comparing the OS distributions of the treatment groups. The hazard ratio (HR) with the associated 95% confidence interval (CI) was reported using Cox proportional hazard regression. The secondary efficacy variables were analyzed using the ITT population. PFS was measured at the EoS. The number and percentage of patients with progression events and deaths were presented. Kaplan-Meier estimates for PFS and the 25th and 75th quartiles were presented by treatment groups. The Kaplan-Meier estimates for PFS at the EoS were also presented by subgroups (different types of SoC). The number and percentage of patients with CR, PR, stable disease (SD), and progressive disease (PD) were presented. In addition, patients with OR and disease control were summarized by count and percentage and the ORR and disease control rate were presented. Kaplan-Meier estimates for PFI_{BIO} and the 25th and 75th quartiles were presented by treatment groups. The CA 125 level at each assessed visit and change from baseline in CA 125 level were summarized using descriptive statistics. An exploratory analysis of QoL was performed using the standardized FACT-O questionnaire.

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

visits.

Safety analyses were performed using the safety population. No statistical analysis for comparing the treatment groups was planned on safety data. AEs were coded using the MedDRA terminology (version 19.1). Severity or intensity of an AE was assessed according to National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.03. All AE tables included only treatment-emergent AEs (TEAEs) unless otherwise noted presented by treatment group and totaled for both treatment groups. A TEAE was an AE that started or worsened (i.e., increased in severity or relationship to study treatment) from the study treatment start date/time to 30 days after the last dose of study treatment (DCVAC/OvCa or SoC). AEs occurring on the day of study treatment start with an unknown start date were also treated as TEAEs. Laboratory measurements were summarized at specified time points for all patients. Changes from baseline were also presented for all continuous parameters. For laboratory tests with NCI CTCAE grading, shift tables were presented to display the shift in grade from baseline to each scheduled assessment.

SUMMARY OF RESULTS AND CONCLUSION

Patient disposition:

The sponsor decided to terminate the enrollment prematurely due to slow recruitment, and only a total of 33 patients were screened in this study. Of the screened patients, 25 patients (75.8%) were randomized and 8 patients (24.2%) were screening failures. Of the 25 randomized patients, 13 patients (52.0%) were randomized to treatment group A (DCVAC/OvCa in addition to SoC) and 12 patients (48.0%) were randomized to treatment group B (SoC alone).

The implications of the data collected in this study are limited due to the low number of randomized and analyzed patients. The sample size was planned to be 60 randomized patients (30 patients per treatment group), and the study and all analyses were designed accordingly. As only 25 patients were randomized, the analysis populations were smaller than planned (the ITT population included 9 patients in treatment group A and 12 patients in treatment group B, the PP population included 2 patients in treatment group A and 5 patients in treatment group B, and the safety population included 12 patients in treatment group A and 10 patients in treatment group B), and, consequently, the statistical analyses did not have sufficient power to estimate the efficacy and safety of DCVAC/OvCa.

Nine of 12 patients (75.0%) included in the safety population of treatment group A were exposed to DCVAC/OvCa. Only 2 of the 12 patients (16.7%) included in the safety population of treatment group A received the planned number of doses of DCVAC/OvCa (i.e., 10 doses); 7 of the 12 patients (58.3%) included in the safety population of treatment group A discontinued DCVAC/OvCa prematurely and received 1 to 6 doses.

Three of 12 patients (25.0%) included in the safety population of treatment group A and 2 of 10 patients (20.0%) included in the safety population of treatment group B were exposed to paclitaxel. Two of 12 patients (16.7%) included in the safety population of treatment group A and 1 of 10 patients (10.0%) included in the safety population of treatment group B were exposed to topotecan. Seven of 12 patients (58.3%) included in the safety population of treatment group A and 7 of 10 patients (70.0%) included in the safety population of treatment group B were exposed to liposomal doxorubicin.

One major protocol deviation was reported in 1 of the 25 randomized patients (4.0%). This major protocol deviation was reported as "Inclusion criteria for WBC and hemoglobin not fulfilled". It occurred in treatment group A and led to study treatment discontinuation and premature termination of the patient's participation in the trial.

Patient demographics and baseline characteristics:

Demographics and oncology history of the two treatment groups were comparable (Table 1, Table 2).

Table 1: Patient demographics, ITT population

	Treatment group A N = 9	**Treatment group B N = 12**
Age: n; median years (min, max)	9; 58.0 (46, 63)	12; 59.0 (33, 76)
Race: n (%): White	9 (100%)	12 (100%)
Weight: n; median kg (min, max)	9; 65.0 (54, 109)	10; 65.5 (49, 89)
Height: n; median cm (min, max)	9; 160.0 (151, 174)	10; 162.5 (152, 175)
BMI: n; median kg/m^2 (min, max)	9; 27.1 (19, 43)	10; 24.4 (18, 33)
BSA: n; median m^2 (min, max)	9; 1.68 (1.5, 2.1)	10; 1.69 (1.5, 2.0)

Table 2: Oncology history, ITT population

	Treatment group A N = 9	**Treatment group B N = 12**
Type of epithelial cells		
Endometrioid, n (%)	1 (11.1%)	-
Mucinous, n (%)	-	1 (8.3%)
Serous, n (%)	8 (88.9%)	11 (91.7%)
FIGO III ovarian cancer stage		
No, n (%)	-	-
Yes, n (%)	9 (100%)	12 (100%)
Time since diagnosis, days		

N	9	9
Mean	347.9	315.1
Standard deviation	72.97	101.01
Median	349.0	342.0
Q1 - Q3	297 - 359	293 - 375
Min - max	243 - 477	126 - 446

Efficacy results:

None of the efficacy analyses showed any statistically significant difference between the treatment groups (OS at the EoS: p = 0.7208, log-rank test [Table 3]; PFS at the EoS: p = 0.2250, log-rank test [Table 4]; PFI_{BIO}: p = 0.1278, log-rank test [Table 5]). The ORR was 0% (95% CI: 0.0, 33.6) in treatment group A and 16.7% (95% CI: 2.1, 48.4) in treatment group B, and the disease control rate was 33.3% (95% CI: 7.5, 70.1) in treatment group A and 16.7% (95% CI: 2.1, 48.4) in treatment group B (Table 6).

Table 3: Primary analysis of OS at the EoS, ITT population

	Treatment group A N = 9	**Treatment group B N = 12**
Patients with death, n (%)	5 (55.6%)	3 (25.0%)
Time to event, days		
25th percentile	180.0	100.0
Median time	206.0	-
75th percentile	-	-
Log-rank test	p = 0.7208	

Table 4: PFS at the EoS, ITT population

	Treatment group A N = 9	**Treatment group B N = 12**
Patients with		
Death, n (%)	1 (11.1%)	2 (16.7%)
Disease progression, n (%)	8 (88.9%)	5 (41.7%)
Time to event, days		
25th percentile	50.0	54.0
Median time	52.0	100.0
75th percentile	162.0	489.0
Log-rank test	p = 0.2250	

Table 5: PFI_{BIO}, ITT population

	Treatment group A N = 9	**Treatment group B N = 12**
Patients with		
Biological disease progression, n (%)	3 (33.3%)	1 (8.3%)
Death, n (%)	1 (11.1%)	2 (16.7%)
Disease progression, n (%)	5 (55.6%)	4 (33.3%)
Time to event (days)		
25th percentile	50.0	54.0
Median time	52.0	100.0
75th percentile	162.0	489.0
Log-rank test	p = 0.1278	

Table 6: ORR, ITT population

	Treatment group A N = 9	**Treatment group B N = 12**
Best overall response		
CR, n (%)	-	1 (8.3%)
PR, n (%)	-	1 (8.3%)

SD, n (%)	3 (33.3%)	-
PD, n (%)	4 (44.4%)	-
Not evaluable, n (%)	2 (22.2%)	10 (83.3%)
OR (CR + PR)	-	2 (16.7%)
Rate	-	16.7%
95% CI (Clopper-Pearson [Exact])	0.0, 33.6	2.1, 48.4
Disease control (CR + PR + SD)	3 (33.3%)	2 (16.7%)
Rate	33.3%	16.7%
95% CI (Clopper-Pearson [Exact])	7.5, 70.1	2.1, 48.4

Exploratory results:

FACT-O questionnaire scores showed that the treatment groups were similar in relation to QoL.

Safety results:

The safety of DCVAC/OvCa was benign. An overall summary of AEs reported in this study is shown in Table 7.

Table 7: Overall summary of AEs, safety population

	Treatment group A N = 12 n (%)	**Treatment group B N = 10 n (%)**
Patients with		
Any TEAEs	10 (83.3%)	9 (90.0%)
DCVAC/OvCa-related TEAEs	-	-
Leukapheresis-related AEs	-	-
SoC-related TEAEs	8 (66.7%)	6 (60.0%)
Serious TEAEs	8 (66.7%)	3 (30.0%)
TEAEs leading to death	3 (25.0%)	1 (10.0%)
TEAEs Grade 3 to 5	8 (66.7%)	3 (30.0%)
TEAEs of special interest	3 (25.0%)	-
TEAEs leading to discontinuation of DCVAC/OvCa	3 (25.0%)	-
TEAEs leading to discontinuation of SoC	5 (41.7%)	1 (10.0%)
TEAEs leading to withdrawal from the study	-	-

The overall incidence of TEAEs seems balanced between the treatment groups, considering the difference in the duration of the TEAE reporting period which was significantly longer in treatment group A (median duration 162.5 days) than in treatment group B (median duration 88.5 days). The most common TEAEs encountered in the trial were signs of bone marrow depression (leukopenia, anemia, neutropenia, and thrombocytopenia), and all were reported as related to SoC for both treatment groups (Table 8).

Table 8: Incidence of TEAEs occurring in ≥2 patients in either treatment group, safety population

Preferred term	**Treatment group A N = 12 n (%)**	**Treatment group B N = 10 n (%)**
Leukopenia	5 (41.7%)	2 (20.0%)
Anaemia	5 (41.7%)	1 (10.0%)
Neutropenia	5 (41.7%)	1 (10.0%)
Thrombocytopenia	5 (41.7%)	-
Abdominal pain	3 (25.0%)	2 (20.0%)
Diarrhoea	3 (25.0%)	2 (20.0%)
Decreased appetite	3 (25.0%)	1 (10.0%)
Ascites	3 (25.0%)	-
Fatigue	2 (16.7%)	1 (10.0%)
General physical health deterioration	2 (16.7%)	1 (10.0%)
Intestinal obstruction	2 (16.7%)	1 (10.0%)
Dyspnoea	2 (16.7%)	-

Ileus	2 (16.7%)	-
Vomiting	2 (16.7%)	-
Cystitis	-	2 (20.0%)
Depression	-	2 (20.0%)

TEAEs leading to deaths were intestinal obstruction (2 and 1 cases in treatment groups A and B, respectively), ileus (1 case in treatment group A), and sepsis (1 case in treatment group A). One patient was reported to encounter 2 of these TEAEs leading to death (a patient in group A experiencing both ileus and sepsis). The underlying causes of these deaths were in all but one case (one case of ileus in treatment group A) determined to be due to ovarian cancer under treatment. No death was reported to be related to DCVAC/OvCa, leukapheresis, or SoC.

The frequency of laboratory abnormalities was similar between the treatment groups.

Conclusion:

Enrollment into this study was stopped prematurely by the sponsor due to slow recruitment, and only 25 patients with ovarian cancer demonstrating incomplete or short-lasting response to Pt-based first-line chemotherapy were randomized. Thus, the implications of the data collected in this study are limited due to the low number of randomized patients. Consequently, the statistical analyses did not have sufficient power to estimate the efficacy and safety of DCVAC/OvCa. The information collected did not indicate any benefit of adding DCVAC/OvCa to SoC versus administering SoC alone. Based on the data obtained, the safety profile of DCVAC/OvCa (including leukapheresis) was benign and did not seem to add any relevant toxicity beyond what was seen for SoC.

DATE AND VERSION OF THIS PUBLIC DISCLOSURE SUMMARY

Version 1.0, 26-Jul-2017