

Supplemental Online Content

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eMethods

eTable 1. Further patient characteristics at baseline, efficacy analysis set

eTable 2. Exposure to DCVAC/PCa or placebo, efficacy analysis set

eTable 3. Post-hoc analysis of overall survival in subgroups of patients who received ≥ 10 , ≥ 12 , and 15 doses of DCVAC/PCa or placebo

eTable 4. Post hoc analysis of patient characteristics at baseline according by number of DCVAC/PCa doses

eTable 5. Secondary endpoints, efficacy analysis set

eTable 6. TEAEs in $\geq 2\%$ of patients in either treatment group, safety analysis set

eFigure 1. Kaplan–Meier estimates of overall survival in subgroups of patients who received ≥ 10 (A), ≥ 12 (B), and 15 doses (C) of DCVAC/PCa plus chemotherapy or placebo plus chemotherapy (post hoc analysis)

eFigure 2. Kaplan–Meier Estimates of Progression-Free Survival, Efficacy Analysis Set

eAppendix 1. List of investigators

eAppendix 2. Serious adverse events

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

The trial was conducted at 176 hospital clinics (3 in Austria, 2 in Belarus, 5 in Belgium, 5 in Bulgaria, 3 in Croatia, 12 in Czech Republic, 1 in Denmark, 6 in France, 19 in Germany, 4 in Hungary, 7 in Italy, 1 in Latvia, 4 in Lithuania, 7 in Netherlands, 6 in Poland, 4 in Portugal, 4 in Serbia, 8 in Slovakia, 11 in Spain, 3 in Sweden, 10 in United Kingdom, and 51 in the US).

Patients were eligible if they had histologically or cytologically confirmed prostate adenocarcinoma and skeletal or soft tissue/visceral/nodal metastases according to (i) confirmed pathological fracture related to the disease; or (ii) confirmed distant bone and/or soft tissue and/or visceral metastases on computed tomography (CT) or magnetic resonance imaging (MRI) scan or bone scintigraphy; or (iii) positive pathology report of metastatic lesion. Patients were required to have experienced disease progression despite ADT and be castrated. Progression was indicated by (i) PSA increase; or (ii) progression of measurable lymph nodes; or (iii) two or more new lesions appearing on bone scan/imaging compared with a previous scan according to the Prostate Cancer Working Group 2 (PCWG2) guidelines.

Patients, investigational site staff, personnel performing the assessments and monitoring, personnel performing leukapheresis, and data analysts were blinded to the identity of the trial treatment from the time of randomization until database lock, using the following methods: (1) randomization data were kept strictly confidential until the time of unblinding, and (2) the identity of the treatments was concealed by leukapheresis in both treatment groups and the use of DCVAC/PCa or placebo that were identical in packaging, labelling, and schedule of administration. Placebo was similar enough in appearance and the syringe was blinded adequately to prevent the patient and blinded staff from knowing the identity of the treatment.

Cell concentrates (60 to 150 mL) containing a minimum of 4×10^9 peripheral blood mononuclear cells were collected. Up to 30 hours after the beginning of leukapheresis, the cells were delivered under controlled conditions to the processing facility of SOTIO a.s., where harvested monocytes of the patients in the DCVAC/PCa group were cultured in the presence of 500 IU/mL recombinant human colony stimulating factor 2 and 248 IU/mL recombinant human interleukin 4 to generate immature DCs (iDCs). iDCs were then pulsed with human LNCaP prostate cancer cells subjected to high hydrostatic pressure for the induction of immunogenic cell death.¹ The LNCaP cell line was selected due to the

expression of a broad panel of prostate-related antigens valuable for cancer vaccine development.² DCs loaded with immunogenic tumor cells were subsequently treated with 25 µg/mL polyinosinic:polycytidylic acid, a Toll-like receptor 3 ligand, to achieve phenotypic and functional maturation. The DCVAC/PCa product was cryopreserved at a concentration of approximately 1×10^7 mature DCs/mL as 1 mL aliquots and stored in liquid nitrogen.

Imaging (CT/MRI of the chest, abdomen, and pelvis and technetium bone scans of the whole body) was performed at screening and after randomization at 12-week intervals (± 7 days). The date of progression, determined centrally by an independent radiologist blinded to treatment assignment according to the PCWG2 recommendations, was used for rPFS evaluation.³

PSA levels were assessed by a central laboratory at screening and then every 12 weeks (± 7 days) as close as possible to imaging time points.

The target sample size (657 deaths) was calculated based on the following assumptions: i) median survival of 24 months for the DCVAC/PCa group and 19 months for the placebo group, exponential survival; ii) 2:1 allocation ratio; iii) $HR M_P/M_{DCVAC}$, where M_{DCVAC} and M_P are the median survival times on DCVAC/PCa and placebo group, respectively, which results in HR 0.792 in favor of the DCVAC/PCa group; and iv) level of significance of 0.05 and 80% power of a two-tailed log-rank test. To reach 657 deaths, 1170 patients were planned to be randomized.

An independent data monitoring committee reviewed key safety data and provided recommendations for continuation or termination of the trial.

References

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doi:10.1200/JCO.2007.12.4487

eTable 1. Further patient characteristics at baseline, efficacy analysis set

	DCVAC/PCa group N = 787	Placebo group N = 395
Age, No. (%)		
<65 years	272 (34.6)	107 (27.1)
≥65 years	515 (65.4)	288 (72.9)
<60 years	110 (14.0)	45 (11.4)
60–69 years	346 (44.0)	159 (40.3)
≥70 years	331 (42.1)	191 (48.4)
Race, No. (%)*		
Asian	5 (0.6)	4 (1.0)
Black or African American	26 (3.3)	19 (4.8)
Native Hawaiian or Other Pacific Islander	1 (0.1)	0
White	733 (93.1)	358 (90.6)
Other	4 (0.5)	3 (0.8)
Unknown	18 (2.3)	11 (2.8)
Ethnicity, No. (%)*		
Hispanic or Latino	22 (2.8)	6 (1.5)
Not Hispanic or Latino	763 (97.0)	388 (98.2)
Unknown	2 (0.3)	1 (0.3)
Weight, kg, median (range) [No.]	87.6 (54.2–175.5) [781]	86.0 (50.0–166.1) [391]
Disease site at baseline, No. (%)		
At least one lesion in liver	55 (7.0)	25 (6.3)
At least one lesion in lungs or other visceral lesions	150 (19.1)	68 (17.2)
Lymph nodes only	66 (8.4)	20 (5.1)
Bone lesions only	291 (37.0)	161 (40.8)
Lymph nodes and bone lesions only	222 (28.2)	121 (30.6)
No lesion	3 (0.4)	0

Site of measurable lesion, <i>No.</i> (%)		
Bone	695 (88.3)	367 (92.9)
Liver	55 (7.0)	25 (6.3)
Lung	83 (10.5)	36 (9.1)
Lymph	400 (50.8)	188 (47.6)
Visceral	97 (12.3)	61 (15.4)
Patients with history of prostate cancer therapy, yes, <i>No.</i> (%)	765 (97.2)	384 (97.2)
Prior treatments, <i>No.</i> (%)		
Abiraterone only	104 (13.2)	64 (16.2)
Enzalutamide only	54 (6.9)	21 (5.3)
Abiraterone and enzalutamide	83 (10.5)	39 (9.9)
Neither abiraterone nor enzalutamide	546 (69.4)	271 (68.6)
Patients with SREs at baseline (or history of), <i>No.</i> (%)	74 (9.4)	33 (8.4)
Stage at diagnosis, <i>No.</i> (%)		
I	38 (4.8)	15 (3.8)
II	118 (15.0)	58 (14.7)
III	192 (24.4)	95 (24.1)
IV	390 (49.6)	197 (49.9)
Missing	49 (6.2)	30 (7.6)
PSA, ng/L, median (range) [<i>No.</i>]	46.4 (0.0–7500.0) [786]	54.0 (0.1–5000.0) [394]
Hemoglobin, g/L, median (range) [<i>No.</i>]	129.0 (84–167) [784]	128.0 (71–163) [393]
Albumin, g/L, median (range) [<i>No.</i>]	43.0 (27–52) [786]	43.0 (30–52) [393]
ALP, IU/L, median (range) [<i>No.</i>]	103.0 (22–2984) [786]	106.0 (24–2323) [393]
LDH, IU/L, median (range) [<i>No.</i>]	199.0 (77–3000) [786]	206.0 (83–1412) [393]
LDH >1 ULN, <i>No.</i> (%)		
Yes	187 (23.8)	93 (23.5)
No	600 (76.2)	302 (76.5)
Risk group based on Gleason score at diagnosis, <i>No.</i> (%)		

Low/very low (score ≤ 6)	95 (12.07)	45 (11.39)
Intermediate (score =7)	246 (31.26)	113 (28.61)
High/very high (score ≥ 8)	431 (54.76)	223 (56.46)
Unknown	15 (1.9)	14 (3.5)
PSA at diagnosis, ng/mL, median (25 th –75 th percentile) [No.]	28.2 (10.0–100.0) [754]	31.1 (11.0–100.0) [366]
≥ 5 ng/mL	695 (88.3)	348 (88.1)
< 5 ng/mL	59 (7.5)	29 (7.3)
Time from prostate adenocarcinoma diagnosis, years, median (range) [No.]	4.0 (0–25) [786]	3.7 (0–32) [395]
Stage at diagnosis, No. (%)		
I	38 (4.8)	15 (3.8)
II	118 (15.0)	58 (14.7)
III	192 (24.4)	95 (24.1)
IV	390 (49.6)	197 (49.9)
Missing	49 (6.2)	30 (7.6)
Measurable disease at screening, No. (%)		
Yes	359 (45.6)	183 (46.3)
No	428 (54.4)	212 (53.7)
Opioid use, No. (%)		
Yes	170 (21.6)	80 (20.3)
No	617 (78.4)	315 (79.7)

*Information was obtained from the patients' medical records

SRE, skeletal-related event; PSA, prostate-specific antigen; ALP, alkaline phosphatase; LDH, lactate dehydrogenase

eTable 2. Exposure to DCVAC/PCa or placebo, efficacy analysis set

	DCVAC/PCa group <i>N</i> = 787	Placebo group <i>N</i> = 395
Patients exposed, <i>No.</i> (%)		
At least one dose ^a	610 (77.5)	376 (95.2)
1 dose	10 (1.3)	8 (2.0)
2 doses	21 (2.7)	9 (2.3)
3 doses	30 (3.8)	22 (5.6)
4 doses	25 (3.2)	3 (0.8)
5 doses	19 (2.4)	18 (4.6)
6 doses	25 (3.2)	12 (3.0)
7 doses	25 (3.2)	13 (3.3)
8 doses	24 (3.0)	18 (4.6)
9 doses	26 (3.3)	26 (6.6)
10 doses	50 (6.4)	29 (7.3)
11 doses	46 (5.8)	26 (6.6)
12 doses	42 (5.3)	20 (5.1)
13 doses	57 (7.2)	26 (6.6)
14 doses	34 (4.3)	22 (5.6)
15 doses	176 (22.4)	123 (31.1)
16 doses	0	1 (0.3) ^b
Doses administered		
Mean (SD)	10.6 (4.3)	10.8 (4.3)
Median (range)	12.0 (1–15)	12.0 (1–16)
Duration of exposure in months		
Mean (SD)	7.7 (3.6)	7.9 (3.6)
Median (range)	8.5 (0.0–15.4)	8.8 (0.0–13.0)

SD, standard deviation

^aLower proportion of patients treated with DCVAC/PCa is due to leukapheresis/manufacturing failures (see **Figure 1** for details)

^bDue to administration error (considered as protocol deviation)

eTable 3. Post-hoc analysis of OS in subgroups of patients who received ≥ 10 , ≥ 12 , or 15 doses of DCVAC/PCa or placebo

	No. of patients (DCVAC/PCa vs placebo)	P-value (log-rank test)	HR (95% CI; Cox regression)	OS medians in months (95% CI; DCVAC/PCa vs placebo)
≥ 10 doses	391 vs 240	0.4760	0.92 (0.74–1.15)	31.5 (29.5–34.0) vs 27.0 (25.5–30.3)
≥ 12 doses	296 vs 186	0.0501	0.77 (0.60–1.00)	35.9 (33.3–38.4) vs 29.8 (25.7–34.9)
15 doses	167 vs 119	0.0914	0.72 (0.49–1.06)	41.2 (36.9–55.7) vs 38.7 (32.1–not estimated) ^a

OS, overall survival; HR, hazard ratio; CI, confidence interval

^aIn the subgroup with 15 doses of DCVAC/PCa or placebo, less than 50% of patients died; therefore, OS 25th percentile 32.1 vs 25.2 months should be considered.

See **eTable 4** for patient characteristics.

eTable 4. Post hoc analysis of patient characteristics at baseline according by number of DCVAC/PCa doses

	≥10 doses N = 631	≥12 doses N = 482	15 doses N = 286
Age, years, median (range) [No.]	68 (46–86) [631]	69 (46–86) [482]	69 (46–86) [286]
Age group 1, No. (%)			
<60 years	84 (13.3)	59 (12.2)	34 (11.9)
60–69 years	272 (43.1)	213 (44.2)	129 (45.1)
≥70 years	275 (43.6)	210 (43.6)	123 (43.0)
Age group 2, No. (%)			
<65 years	201 (31.9)	153 (31.7)	93 (32.5)
≥65 years	430 (68.1)	329 (68.3)	193 (67.5)
Race, No. (%)			
Asian	4 (0.6)	2 (0.4)	2 (0.7)
Black or African American	20 (3.2)	11 (2.3)	7 (2.5)
Native Hawaiian or Other Pacific Islander	1 (0.2)	0	0
White	587 (95.3)	458 (96.8)	272 (96.5)
Other	4 (0.6)	2 (0.4)	1 (0.4)
Ethnicity, No. (%)			
Hispanic or Latino	13 (2.1)	9 (1.9)	3 (1.0)
Not Hispanic or Latino	617 (97.9)	472 (98.1)	283 (99.0)
Weight, kg, median (range) [No.]	87.4 (52–176) [628]	87.0 (54–176) [479]	87.9 (56–176) [284]
ECOG category, No. (%)			
0	418 (66.2)	326 (67.6)	198 (69.2)
1	205 (32.5)	150 (31.1)	84 (29.4)
0 or 1	623 (98.7)	476 (98.8)	282 (98.6)
2	8 (1.3)	6 (1.2)	4 (1.4)

PSA, ng/L, median (range) [No.]	59.1 (0.0–7689.0) [631]	53.5 (0.0–5000.0) [482]	37.8 (0.0–5000.0) [286]
Disease site at baseline, No. (%)			
At least one lesion in liver	26 (4.1)	16 (3.3)	6 (2.1)
At least one lesion in lungs or other visceral lesions	102 (16.2)	78 (16.2)	48 (16.8)
Lymph nodes only	52 (8.2)	41 (8.5)	26 (9.1)
Bone lesions only	269 (42.6)	216 (44.8)	139 (48.6)
Lymph nodes and bone lesions only	180 (28.5)	130 (27.0)	67 (23.4)
No lesion	2 (0.3)	1 (0.2)	0
Region, No. (%)			
US	92 (14.6)	62 (12.9)	31 (10.8)
Non-US	539 (85.4)	420 (87.1)	255 (89.2)
Prior treatment with abiraterone and/or enzalutamide, No. (%)			
Abiraterone only	134 (21.2)	93 (19.3)	44 (15.4)
Enzalutamide only	89 (14.1)	60 (12.4)	27 (9.4)
Abiraterone and enzalutamide	54 (8.6)	39 (8.1)	19 (6.6)
Neither abiraterone nor enzalutamide	462 (73.2)	368 (76.3)	234 (81.8)
Patients with SREs at baseline (or history of), No. (%)	49 (7.8)	35 (7.3)	17 (5.9)

Gleason score at diagnosis, <i>No.</i> (%)			
8–10	346 (54.8)	264 (54.8)	144 (50.3)
<8	275 (43.6)	212 (44.0)	140 (49.0)
Unknown	10 (1.6)	6 (1.2)	2 (0.7)
PSA at diagnosis, ng/mL, median (25 th –75 th percentile) [<i>No.</i>]	29.4 (9.9–100.0) [610]	30.5 (10.0–100.0) [466]	32.0 (11.2–100.0) [278]
≥ 5 ng/mL	559 (88.6)	429 (89.0)	263 (92.0)
< 5 ng/mL	51 (8.1)	37 (7.7)	15 (5.2)
Time from prostate adenocarcinoma diagnosis, years, median (range) [<i>No.</i>]	4.2 (0–25) [631]	4.3 (0–25) [482]	4.4 (0–25) [286]
Stage at diagnosis, <i>No.</i> (%)			
I	21 (3.3)	15 (3.1)	7 (2.4)
II	99 (15.7)	68 (14.1)	41 (14.3)
III	169 (26.8)	136 (28.2)	83 (29.0)
IV	304 (48.2)	233 (48.3)	139 (48.6)
Missing	38 (6.0)	30 (6.2)	16 (5.6)

ECOG, Eastern Cooperative Oncology Group; PSA, prostate-specific antigen; US, United States; SRE, skeletal-related event

eTable 5. Secondary endpoints, efficacy analysis set

	<i>P</i>-value (log-rank test)	HR (95% CI; Cox regression)	Medians in months (95% CI; DCVAC/PCa vs placebo)
rPFS	0.886	0.99 (0.86–1.14)	11.1 (11.0–11.4) vs 11.1 (10.8–11.4)
Time to PSA progression	0.392	1.08 (0.91–1.28)	10.5 (9.7–10.6) vs 10.6 (10.4–10.7)
Time to the first SRE	0.732	0.92 (0.56–1.50)	Not reached
Time to radiographic progression or SRE	0.111	0.90 (0.78–1.03)	11.1 (10.9–11.3) vs 10.9 (10.5–11.2)
	<i>P</i>-value	Relative risk (95% CI)	Proportion of patients with ≥1 SRE (DCVAC/PCa vs placebo)
Proportion of patients with SREs	0.485	0.85 (0.53–1.36)	0.05 vs 0.07

HR, hazard ratio; CI, confidence interval; rPFS, radiological progression-free survival; PSA, prostate-specific antigen; SRE, skeletal-related event

eTable 6. TEAEs reported in $\geq 2\%$ of patients in either treatment group

No. (%)	DCVAC/PCa group N = 749	Placebo group N = 379
Fatigue	271 (36.2)	152 (40.1)
Alopecia	222 (29.6)	130 (34.3)
Diarrhea	206 (27.5)	117 (30.9)
Nausea	151 (20.2)	96 (25.3)
Anemia	129 (17.2)	77 (20.3)
Edema peripheral	121 (16.2)	88 (23.2)
Back pain	116 (15.5)	67 (17.7)
Arthralgia	115 (15.4)	75 (19.8)
Neutropenia	113 (15.1)	57 (15.0)
Constipation	112 (15.0)	71 (18.7)
Decreased appetite	111 (14.8)	79 (20.8)
Asthenia	109 (14.6)	70 (18.5)
Pain in extremity	87 (11.6)	55 (14.5)
Neuropathy peripheral	84 (11.2)	55 (14.5)
Pyrexia	84 (11.2)	46 (12.1)
Dyspnea	82 (10.9)	56 (14.8)
Cough	82 (10.9)	47 (12.4)
Dysgeusia	80 (10.7)	59 (15.6)
Bone pain	79 (10.5)	27 (7.1)
Vomiting	78 (10.4)	44 (11.6)
Paresthesia	76 (10.1)	33 (8.7)
Leukopenia	64 (8.5)	35 (9.2)
Urinary tract infection	60 (8.0)	43 (11.3)
Hyperglycemia	56 (7.5)	27 (7.1)
Myalgia	53 (7.1)	32 (8.4)
Musculoskeletal pain	47 (6.3)	24 (6.3)
Weight decreased	46 (6.1)	24 (6.3)
Polyneuropathy	44 (5.9)	24 (6.3)

Dyspepsia	44 (5.9)	22 (5.8)
Hypertension	43 (5.7)	35 (9.2)
Dizziness	41 (5.5)	33 (8.7)
Hypotension	41 (5.5)	28 (7.4)
Stomatitis	39 (5.2)	25 (6.6)
Nail disorder	38 (5.1)	28 (7.4)
Pneumonia	38 (5.1)	21 (5.5)
Febrile neutropenia	37 (4.9)	34 (9.0)
Peripheral sensory neuropathy	37 (4.9)	28 (7.4)
Taste disorder	37 (4.9)	21 (5.5)
Epistaxis	37 (4.9)	17 (4.5)
Rash	36 (4.8)	22 (5.8)
Hematuria	36 (4.8)	18 (4.7)
Headache	35 (4.7)	27 (7.1)
Dehydration	35 (4.7)	14 (3.7)
Upper respiratory tract infection	34 (4.5)	20 (5.3)
Nasopharyngitis	33 (4.4)	22 (5.8)
Insomnia	32 (4.3)	24 (6.3)
Muscular weakness	32 (4.3)	23 (6.1)
Hypoesthesia	32 (4.3)	20 (5.3)
Onycholysis	31 (4.1)	18 (4.7)
Influenza like illness	30 (4.0)	14 (3.7)
Peripheral swelling	30 (4.0)	11 (2.9)
Lacrimation increased	29 (3.9)	30 (7.9)
Abdominal pain	29 (3.9)	23 (6.1)
Hypokalemia	29 (3.9)	17 (4.5)
Mucosal inflammation	28 (3.7)	22 (5.8)
Muscle spasms	26 (3.5)	10 (2.6)
Oropharyngeal pain	26 (3.5)	9 (2.4)
Spinal pain	26 (3.5)	9 (2.4)
Pulmonary embolism	25 (3.3)	18 (4.7)

Nail discoloration	25 (3.3)	17 (4.5)
Erythema	25 (3.3)	13 (3.4)
Tachycardia	25 (3.3)	12 (3.2)
Atrial fibrillation	25 (3.3)	9 (2.4)
Dry skin	23 (3.1)	18 (4.7)
Thrombocytopenia	23 (3.1)	6 (1.6)
Neutrophil count decreased	22 (2.9)	18 (4.7)
Nail dystrophy	22 (2.9)	16 (4.2)
Fall	22 (2.9)	12 (3.2)
General physical health deterioration	21 (2.8)	10 (2.6)
Hypocalcemia	21 (2.8)	9 (2.4)
Palmar-plantar erythrodysesthesia syndrome	21 (2.8)	9 (2.4)
Bronchitis	20 (2.7)	14 (3.7)
White blood cell count decreased	20 (2.7)	13 (3.4)
Depression	20 (2.7)	11 (2.9)
Musculoskeletal chest pain	20 (2.7)	11 (2.9)
Urinary retention	19 (2.5)	16 (4.2)
Abdominal pain upper	19 (2.5)	15 (4.0)
Hot flush	19 (2.5)	11 (2.9)
Gastroesophageal reflux disease	17 (2.3)	6 (1.6)
Syncope	16 (2.1)	12 (3.2)
Blood creatinine increased	16 (2.1)	11 (2.9)
Toothache	16 (2.1)	7 (1.8)
Vertigo	15 (2.0)	14 (3.7)
Dry mouth	15 (2.0)	12 (3.2)
Cancer pain	15 (2.0)	10 (2.6)
Blood alkaline phosphatase increased	15 (2.0)	9 (2.4)
Deep vein thrombosis	15 (2.0)	9 (2.4)
Pain	15 (2.0)	8 (2.1)
Acute kidney injury	15 (2.0)	7 (1.8)

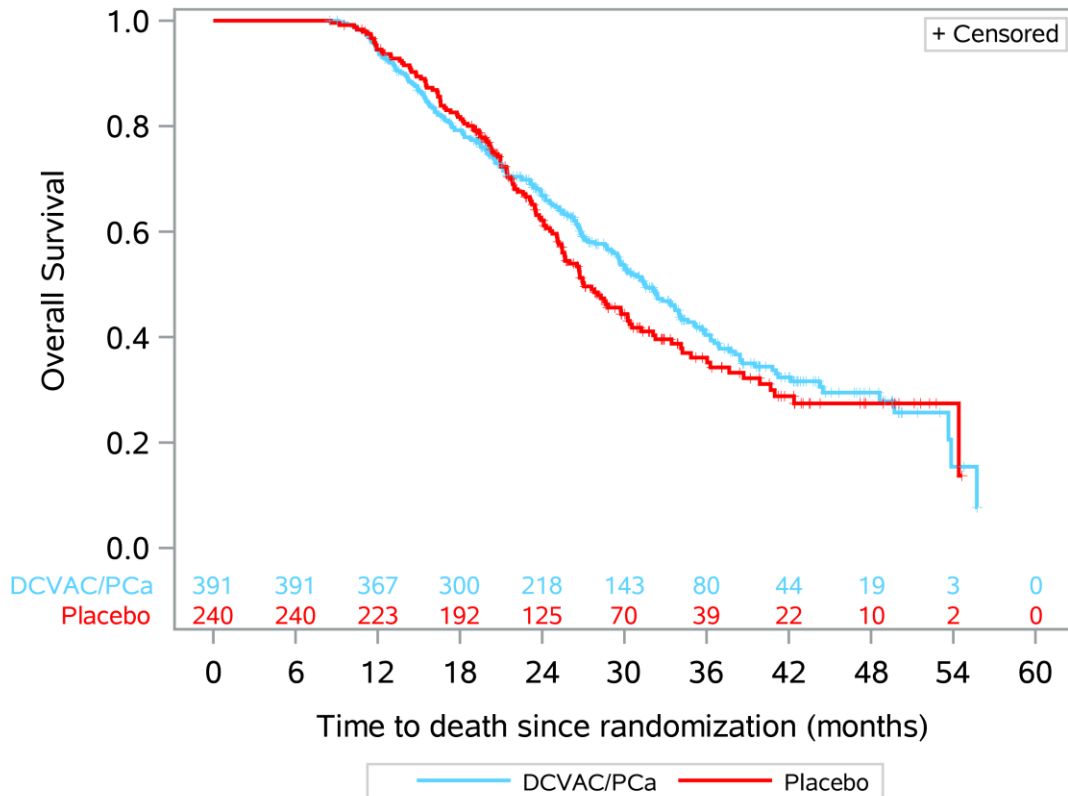
Rhinorrhea	14 (1.9)	16 (4.2)
Anxiety	14 (1.9)	12 (3.2)
Leukocytosis	14 (1.9)	12 (3.2)
Oedema	14 (1.9)	9 (2.4)
Hyponatremia	14 (1.9)	8 (2.1)
Rhinitis	13 (1.7)	15 (4.0)
Pruritus	13 (1.7)	10 (2.6)
Dysuria	13 (1.7)	9 (2.4)
Contusion	13 (1.7)	8 (2.1)
Dysphonia	13 (1.7)	8 (2.1)
Hydronephrosis	13 (1.7)	8 (2.1)
Oral candidiasis	12 (1.6)	11 (2.9)
Pelvic pain	12 (1.6)	9 (2.4)
Urinary incontinence	12 (1.6)	9 (2.4)
Influenza	12 (1.6)	8 (2.1)
C-reactive protein increased	11 (1.5)	9 (2.4)
Lymphopenia	11 (1.5)	9 (2.4)
Ageusia	11 (1.5)	8 (2.1)
Hemorrhoids	11 (1.5)	8 (2.1)
Pollakiuria	10 (1.3)	9 (2.4)
Hyperkalemia	9 (1.2)	10 (2.6)
Injection site reaction	9 (1.2)	8 (2.1)
Pleural effusion	8 (1.1)	12 (3.2)
Weight increased	8 (1.1)	9 (2.4)
Malaise	8 (1.1)	8 (2.1)
Onychomadesis	7 (0.9)	9 (2.4)

TEAEs in bold font occurred in $\geq 10\%$ of patients in either group

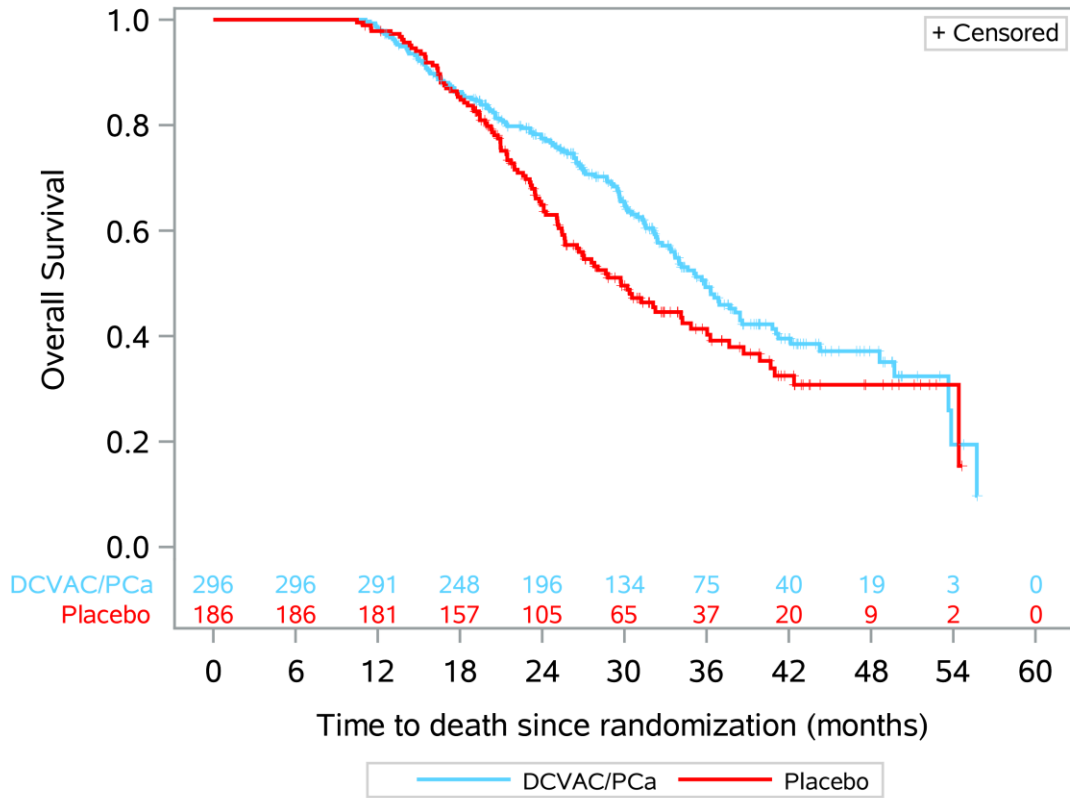
TEAE, treatment-emergent adverse event

eFigure 1. Kaplan–Meier estimates of overall survival in subgroups of patients who received ≥ 10 (A), ≥ 12 (B), and 15 doses (C) of DCVAC/PCa plus chemotherapy or placebo plus chemotherapy (post hoc analysis)

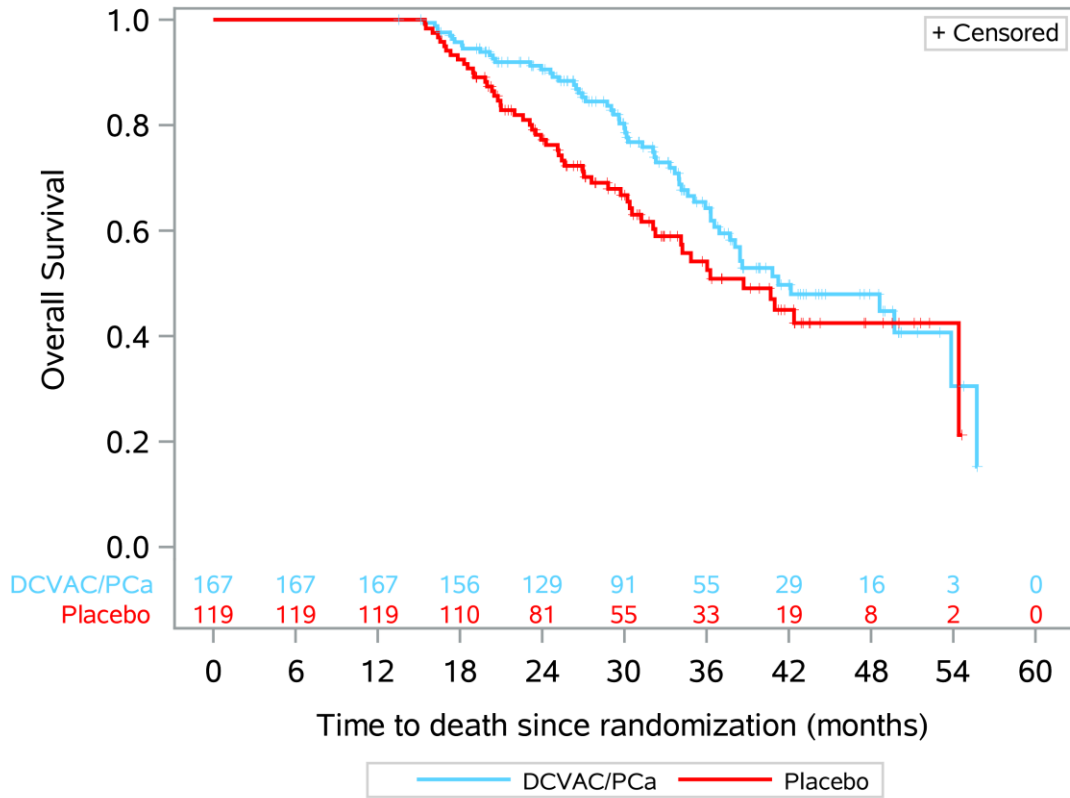
A



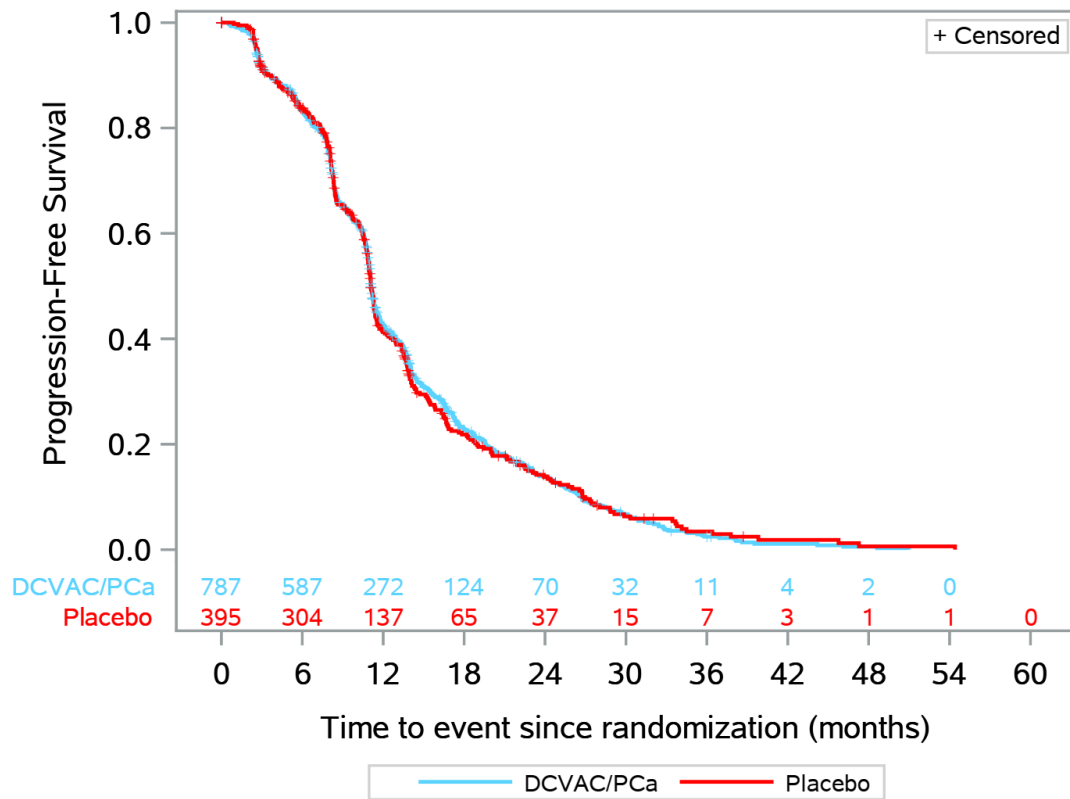
B



C



eFigure 2. Kaplan–Meier Estimates of Progression-Free Survival, Efficacy Analysis Set



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eAppendix 2. Serious adverse events

AE Table 1 Summary of Serious Treatment Emergent Adverse Events
(Safety Population)

	DCVAC/PCa group+ Chemotherapy (N=749)			Placebo group+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Any SAE	237	(31.6)	439	150	(39.6)	273	387	(34.3)	712
Patients Discontinued Study Due to an SAE	6	(0.8)	6	4	(1.1)	4	10	(0.9)	10
SAEs related to DCVAC/PCa or Placebo	9	(1.2)	14	11	(2.9)	13	20	(1.8)	27
SAEs related to Standard Care Chemotherapy	108	(14.4)	146	76	(20.1)	117	184	(16.3)	263
SAEs related to Leukapheresis	0			0			0		
Special-Interest SAEs	23	(3.1)	25	13	(3.4)	14	36	(3.2)	39
Serious Skeletal Related Events	10	(1.3)	13	4	(1.1)	4	14	(1.2)	17
Injection Site Reaction events	0			1	(0.3)	1	1	(0.1)	1
SAEs leading to action taken with IMP									
Delay Of Further Application	62	(8.3)	87	39	(10.3)	56	101	(9.0)	143
Study Drug Permanently Discontinued	18	(2.4)	18	11	(2.9)	12	29	(2.6)	30
Other	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Not Applicable	199	(26.6)	333	125	(33.0)	204	324	(28.7)	537

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Page 1 of 3

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Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

Notes: [1] All treatment emergent serious adverse events are included in summary statistics.

[2] Related refers to events with a suspected or an unknown relationship.

[3] If a patient has multiple events of the same severity, relationship or outcome, then they are counted only once in that severity, relationship or outcome. However, patients can be counted more than once overall.

[4] Table presents number and percentage of patients (n(%)) and number of events (E).

[5] Percentages are based on the number of patients in the respective treatment arm.

[6] SAEs related to Leukapheresis are not emergent to the treatment

[7] In case of several episodes of the same AE the AE will be counted only once (with worst CTC grade, action taken with IMP/chemo, seriousness, causality; the outcome of the last episode will be remained).

[8] AESI(Special-Interest AEs) are identified only for SAEs

AE Table 1 Summary of Serious Treatment Emergent Adverse Events
(Safety Population)

	DCVAC/PCa group+ Chemotherapy (N=749)			Placebo group+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Chemotherapy									
Application interrupted	0			0			0		
Delayed	45	(6.0)	58	24	(6.3)	34	69	(6.1)	92
Discontinued	30	(4.0)	36	18	(4.7)	20	48	(4.3)	56
Dosage modified	22	(2.9)	22	21	(5.5)	22	43	(3.8)	44
Other	1	(0.1)	2	2	(0.5)	2	3	(0.3)	4
Not Applicable	185	(24.7)	321	120	(31.7)	195	305	(27.0)	516
SAE Severity									
Grade 1: Mild	11	(1.5)	13	8	(2.1)	8	19	(1.7)	21
Grade 2: Moderate	49	(6.5)	62	33	(8.7)	39	82	(7.3)	101
Grade 3: Severe	175	(23.4)	279	111	(29.3)	183	286	(25.4)	462
Grade 4: Life-threatening/Disabling	46	(6.1)	57	23	(6.1)	26	69	(6.1)	83
Grade 5: Death	28	(3.7)	28	17	(4.5)	17	45	(4.0)	45

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Page 2 of 3

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AE Table 1 Summary of Serious Treatment Emergent Adverse Events
(Safety Population)

	DCVAC/PCa group+ Chemotherapy (N=749)			Placebo group+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
SAE Outcome									
Not Recovered/Not Resolved	32	(4.3)	37	18	(4.7)	20	50	(4.4)	57
Recovering/Resolving	5	(0.7)	6	3	(0.8)	5	8	(0.7)	11
Recovered/Resolved With Sequelae	7	(0.9)	8	4	(1.1)	4	11	(1.0)	12
Recovered/Resolved	204	(27.2)	351	123	(32.5)	224	327	(29.0)	575
Fatal	28	(3.7)	31	17	(4.5)	18	45	(4.0)	49
Unknown	4	(0.5)	6	2	(0.5)	2	6	(0.5)	8

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Page 3 of 3

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Notes: [1] All treatment emergent serious adverse events are included in summary statistics.

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[3] If a patient has multiple events of the same severity, relationship or outcome, then they are counted only once in that severity, relationship or outcome. However, patients can be counted more than once overall.

[4] Table presents number and percentage of patients (n(%)) and number of events (E).

[5] Percentages are based on the number of patients in the respective treatment arm.

[6] SAEs related to Leukapheresis are not emergent to the treatment

[7] In case of several episodes of the same AE the AE will be counted only once (with worst CTC grade, action taken with IMP/chemo, seriousness, causality; the outcome of the last episode will be remained).

[8] AESI(Special-Interest AEs) are identified only for SAEs

AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)		Placebo+ Chemotherapy (N=379)		Overall (N=1128)	
	n (%)	E	n (%)	E	n (%)	E
Any AE	237 (31.6)	439	150 (39.6)	273	387 (34.3)	712
Infections and infestations	74 (9.9)	94	48 (12.7)	62	122 (10.8)	156
Pneumonia	18 (2.4)	18	11 (2.9)	13	29 (2.6)	31
Urinary tract infection	10 (1.3)	13	8 (2.1)	9	18 (1.6)	22
Sepsis	8 (1.1)	8	5 (1.3)	5	13 (1.2)	13
Neutropenic sepsis	7 (0.9)	7	5 (1.3)	7	12 (1.1)	14
Bronchitis	2 (0.3)	2	2 (0.5)	2	4 (0.4)	4
Infection	3 (0.4)	3	1 (0.3)	1	4 (0.4)	4
Cellulitis	3 (0.4)	3	0		3 (0.3)	3
Urosepsis	3 (0.4)	3	0		3 (0.3)	3
Anal abscess	1 (0.1)	1	1 (0.3)	1	2 (0.2)	2
Clostridium difficile colitis	2 (0.3)	2	0		2 (0.2)	2
Clostridium difficile infection	1 (0.1)	1	1 (0.3)	1	2 (0.2)	2
Device related infection	1 (0.1)	1	1 (0.3)	1	2 (0.2)	2
Escherichia sepsis	1 (0.1)	1	1 (0.3)	1	2 (0.2)	2
Gastroenteritis	2 (0.3)	2	0		2 (0.2)	2
Herpes zoster	0		2 (0.5)	2	2 (0.2)	2
Influenza	1 (0.1)	1	1 (0.3)	1	2 (0.2)	2
Lower respiratory tract infection	0		2 (0.5)	2	2 (0.2)	2

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Page 1 of 16

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Notes: [1] If a patient has multiple occurrences of an AE, the patient is presented only once in the patient count.

[2] Table presents number and percentage of patients (n (%)) and number of events (E).

[3] Percentages are based on the number of patients in the respective treatment arm.

[4] In case of several episodes of the same AE the AE will be counted only once (with worst CTC grade, action taken with IMP/chemo, seriousness, causality; the outcome of the last episode will be remained).

AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Infections and infestations (cont.)									
Osteomyelitis	2	(0.3)	2	0			2	(0.2)	2
Peritonitis	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Pyelonephritis	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Respiratory tract infection	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Staphylococcal bacteraemia	2	(0.3)	2	0			2	(0.2)	2
Staphylococcal sepsis	2	(0.3)	2	0			2	(0.2)	2
Abscess soft tissue	1	(0.1)	2	0			1	(0.1)	2
Abdominal infection	0			1	(0.3)	1	1	(0.1)	1
Abscess limb	0			1	(0.3)	1	1	(0.1)	1
Abscess oral	1	(0.1)	1	0			1	(0.1)	1
Appendicitis	1	(0.1)	1	0			1	(0.1)	1
Biliary tract infection	0			1	(0.3)	1	1	(0.1)	1
Catheter site cellulitis	1	(0.1)	1	0			1	(0.1)	1
Cellulitis orbital	1	(0.1)	1	0			1	(0.1)	1
Cholangitis infective	0			1	(0.3)	1	1	(0.1)	1
Complicated appendicitis	1	(0.1)	1	0			1	(0.1)	1
Cytomegalovirus infection	0			1	(0.3)	1	1	(0.1)	1
Cytomegalovirus oesophagitis	0			1	(0.3)	1	1	(0.1)	1
Dermo-hypodermatitis	0			1	(0.3)	1	1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 2 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Infections and infestations (cont.)									
Device related sepsis	1	(0.1)	1	0			1	(0.1)	1
Diverticulitis	1	(0.1)	1	0			1	(0.1)	1
Enterococcal bacteraemia	0			1	(0.3)	1	1	(0.1)	1
Enterocolitis infectious	1	(0.1)	1	0			1	(0.1)	1
Erysipelas	1	(0.1)	1	0			1	(0.1)	1
Gastroenteritis norovirus	0			1	(0.3)	1	1	(0.1)	1
Gastroenteritis viral	0			1	(0.3)	1	1	(0.1)	1
Paraspinal abscess	1	(0.1)	1	0			1	(0.1)	1
Perirectal abscess	1	(0.1)	1	0			1	(0.1)	1
Pneumonia mycoplasmal	1	(0.1)	1	0			1	(0.1)	1
Pneumonia viral	0			1	(0.3)	1	1	(0.1)	1
Rectal abscess	1	(0.1)	1	0			1	(0.1)	1
Septic shock	1	(0.1)	1	0			1	(0.1)	1
Staphylococcal abscess	0			1	(0.3)	1	1	(0.1)	1
Streptococcal sepsis	0			1	(0.3)	1	1	(0.1)	1
Tracheobronchitis	1	(0.1)	1	0			1	(0.1)	1
Urinary tract infection staphylococcal	1	(0.1)	1	0			1	(0.1)	1
Viral sepsis	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 3 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Blood and lymphatic system disorders	50	(6.7)	60	36	(9.5)	48	86	(7.6)	108
Febrile neutropenia	25	(3.3)	27	29	(7.7)	34	54	(4.8)	61
Neutropenia	12	(1.6)	12	5	(1.3)	7	17	(1.5)	19
Anaemia	9	(1.2)	14	3	(0.8)	3	12	(1.1)	17
Leukopenia	2	(0.3)	3	2	(0.5)	2	4	(0.4)	5
Pancytopenia	4	(0.5)	4	0			4	(0.4)	4
Agranulocytosis	0			1	(0.3)	1	1	(0.1)	1
Bicytopenia	0			1	(0.3)	1	1	(0.1)	1
Respiratory, thoracic and mediastinal disorders	37	(4.9)	45	22	(5.8)	24	59	(5.2)	69
Pulmonary embolism	18	(2.4)	18	15	(4.0)	15	33	(2.9)	33
Acute respiratory failure	4	(0.5)	4	2	(0.5)	2	6	(0.5)	6
Interstitial lung disease	2	(0.3)	3	3	(0.8)	3	5	(0.4)	6
Pneumonia aspiration	2	(0.3)	2	2	(0.5)	2	4	(0.4)	4
Pneumonitis	3	(0.4)	3	1	(0.3)	1	4	(0.4)	4
Respiratory failure	4	(0.5)	4	0			4	(0.4)	4
Pleural effusion	3	(0.4)	3	0			3	(0.3)	3
Chronic obstructive pulmonary disease	2	(0.3)	2	0			2	(0.2)	2
Acute respiratory distress syndrome	1	(0.1)	1	0			1	(0.1)	1
Dyspnoea	0			1	(0.3)	1	1	(0.1)	1

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Produced: 19 June 2020, 11:41

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Respiratory, thoracic and mediastinal disorders (cont.)									
Dyspnoea exertional	1	(0.1)	1	0			1	(0.1)	1
Hydrothorax	1	(0.1)	1	0			1	(0.1)	1
Hypoxia	1	(0.1)	1	0			1	(0.1)	1
Pulmonary fibrosis	1	(0.1)	1	0			1	(0.1)	1
Pulmonary oedema	1	(0.1)	1	0			1	(0.1)	1
General disorders and administration site conditions									
Pyrexia	33	(4.4)	37	16	(4.2)	22	49	(4.3)	59
Death	9	(1.2)	13	6	(1.6)	9	15	(1.3)	22
Fatigue	5	(0.7)	5	5	(1.3)	5	10	(0.9)	10
General physical health deterioration	5	(0.7)	5	1	(0.3)	1	6	(0.5)	6
Asthenia	6	(0.8)	6	0			6	(0.5)	6
Systemic inflammatory response syndrome	3	(0.4)	3	1	(0.3)	1	4	(0.4)	4
Oedema peripheral	0			3	(0.8)	4	3	(0.3)	4
Catheter site inflammation	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Chest pain	1	(0.1)	1	0			1	(0.1)	1
Complication associated with device	1	(0.1)	1	0			1	(0.1)	1
Non-cardiac chest pain	0			1	(0.3)	1	1	(0.1)	1
Sudden death	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 5 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Gastrointestinal disorders	23	(3.1)	27	23	(6.1)	35	46	(4.1)	62
Diarrhoea	5	(0.7)	5	5	(1.3)	6	10	(0.9)	11
Vomiting	2	(0.3)	2	4	(1.1)	6	6	(0.5)	8
Nausea	1	(0.1)	1	3	(0.8)	4	4	(0.4)	5
Constipation	2	(0.3)	2	1	(0.3)	1	3	(0.3)	3
Abdominal pain	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Gastric ulcer haemorrhage	0			2	(0.5)	2	2	(0.2)	2
Intestinal obstruction	2	(0.3)	2	0			2	(0.2)	2
Large intestine perforation	0			2	(0.5)	2	2	(0.2)	2
Oesophagitis	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Pancreatitis acute	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Abdominal pain upper	0			1	(0.3)	1	1	(0.1)	1
Colitis ischaemic	1	(0.1)	1	0			1	(0.1)	1
Dysphagia	0			1	(0.3)	1	1	(0.1)	1
Enterocolitis haemorrhagic	1	(0.1)	1	0			1	(0.1)	1
Gastric antral vascular ectasia	0			1	(0.3)	1	1	(0.1)	1
Gastric haemorrhage	1	(0.1)	1	0			1	(0.1)	1
Gastric ulcer	0			1	(0.3)	1	1	(0.1)	1
Gastric ulcer perforation	1	(0.1)	1	0			1	(0.1)	1
Gastritis	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 6 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Gastrointestinal disorders (cont.)									
Gastrointestinal haemorrhage	1	(0.1)	1	0			1	(0.1)	1
Gastrointestinal inflammation	0			1	(0.3)	1	1	(0.1)	1
Haematochezia	1	(0.1)	1	0			1	(0.1)	1
Haemorrhoidal haemorrhage	1	(0.1)	1	0			1	(0.1)	1
Ileus	0			1	(0.3)	1	1	(0.1)	1
Obstructive pancreatitis	0			1	(0.3)	1	1	(0.1)	1
Pancreatitis	1	(0.1)	1	0			1	(0.1)	1
Peptic ulcer	0			1	(0.3)	1	1	(0.1)	1
Rectal haemorrhage	1	(0.1)	1	0			1	(0.1)	1
Rectal perforation	0			1	(0.3)	1	1	(0.1)	1
Small intestinal haemorrhage	1	(0.1)	1	0			1	(0.1)	1
Small intestinal obstruction	1	(0.1)	1	0			1	(0.1)	1
Small intestinal stenosis	0			1	(0.3)	1	1	(0.1)	1
Stomatitis	0			1	(0.3)	1	1	(0.1)	1
Nervous system disorders									
Syncope	31	(4.1)	33	12	(3.2)	14	43	(3.8)	47
Ischaemic stroke	7	(0.9)	8	3	(0.8)	3	10	(0.9)	11
Neuropathy peripheral	3	(0.4)	3	2	(0.5)	3	5	(0.4)	6
	1	(0.1)	1	2	(0.5)	2	3	(0.3)	3

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 7 of 16

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	n	(%)	E	n	(%)	E	n	(%)	E
Nervous system disorders (cont.)									
Spinal cord compression	2	(0.3)	2	1	(0.3)	1	3	(0.3)	3
Cerebral haemorrhage	2	(0.3)	2	0			2	(0.2)	2
Cerebrovascular accident	2	(0.3)	2	0			2	(0.2)	2
Transient ischaemic attack	2	(0.3)	2	0			2	(0.2)	2
Amnesia	0			1	(0.3)	1	1	(0.1)	1
Brain injury	1	(0.1)	1	0			1	(0.1)	1
Cauda equina syndrome	1	(0.1)	1	0			1	(0.1)	1
Cerebral infarction	0			1	(0.3)	1	1	(0.1)	1
Cerebral venous thrombosis	1	(0.1)	1	0			1	(0.1)	1
Diabetic coma	0			1	(0.3)	1	1	(0.1)	1
Ischaemic cerebral infarction	1	(0.1)	1	0			1	(0.1)	1
Loss of consciousness	1	(0.1)	1	0			1	(0.1)	1
Monoparesis	1	(0.1)	1	0			1	(0.1)	1
Paraparesis	1	(0.1)	1	0			1	(0.1)	1
Paraplegia	0			1	(0.3)	1	1	(0.1)	1
Peripheral motor neuropathy	0			1	(0.3)	1	1	(0.1)	1
Peripheral sensory neuropathy	1	(0.1)	1	0			1	(0.1)	1
Polyneuropathy	1	(0.1)	1	0			1	(0.1)	1
Sciatica	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 8 of 16

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	n	(%)	E	n	(%)	E	n	(%)	E
Nervous system disorders (cont.)									
Seizure	1	(0.1)	1	0			1	(0.1)	1
Superior sagittal sinus thrombosis	1	(0.1)	1	0			1	(0.1)	1
Vertigo CNS origin	1	(0.1)	1	0			1	(0.1)	1
Renal and urinary disorders									
Urinary retention	24	(3.2)	34	13	(3.4)	15	37	(3.3)	49
Acute kidney injury	7	(0.9)	8	4	(1.1)	5	11	(1.0)	13
Hydronephrosis	5	(0.7)	5	4	(1.1)	4	9	(0.8)	9
Haematuria	6	(0.8)	6	2	(0.5)	2	8	(0.7)	8
Renal failure	6	(0.8)	8	0			6	(0.5)	8
Urinary tract obstruction	3	(0.4)	3	1	(0.3)	1	4	(0.4)	4
Calculus bladder	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Chronic kidney disease	1	(0.1)	1	0			1	(0.1)	1
Renal atrophy	0			1	(0.3)	1	1	(0.1)	1
Renal impairment	0			1	(0.3)	1	1	(0.1)	1
Ureterolithiasis	1	(0.1)	1	0			1	(0.1)	1
Cardiac disorders									
Atrial fibrillation	17	(2.3)	23	15	(4.0)	16	32	(2.8)	39
	7	(0.9)	8	2	(0.5)	2	9	(0.8)	10

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 9 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

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	n	(%)	E	n	(%)	E	n	(%)	E
Cardiac disorders (cont.)									
Cardiac failure	2	(0.3)	2	2	(0.5)	2	4	(0.4)	4
Myocardial infarction	3	(0.4)	3	1	(0.3)	1	4	(0.4)	4
Cardiac failure congestive	1	(0.1)	1	2	(0.5)	2	3	(0.3)	3
Acute myocardial infarction	0			2	(0.5)	2	2	(0.2)	2
Atrioventricular block	2	(0.3)	2	0			2	(0.2)	2
Cardiac failure chronic	0			2	(0.5)	2	2	(0.2)	2
Angina pectoris	1	(0.1)	1	0			1	(0.1)	1
Aortic valve stenosis	0			1	(0.3)	1	1	(0.1)	1
Atrial flutter	1	(0.1)	1	0			1	(0.1)	1
Atrial tachycardia	0			1	(0.3)	1	1	(0.1)	1
Cardiac arrest	0			1	(0.3)	1	1	(0.1)	1
Cardiac failure acute	1	(0.1)	1	0			1	(0.1)	1
Cardiogenic shock	1	(0.1)	1	0			1	(0.1)	1
Cardiomyopathy	0			1	(0.3)	1	1	(0.1)	1
Coronary artery disease	1	(0.1)	1	0			1	(0.1)	1
Myocarditis	0			1	(0.3)	1	1	(0.1)	1
Tachycardia	1	(0.1)	1	0			1	(0.1)	1
Ventricular extrasystoles	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 10 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Musculoskeletal and connective tissue disorders	19	(2.5)	20	10	(2.6)	11	29	(2.6)	31
Back pain	7	(0.9)	7	1	(0.3)	1	8	(0.7)	8
Osteonecrosis of jaw	5	(0.7)	5	1	(0.3)	1	6	(0.5)	6
Bone pain	1	(0.1)	1	2	(0.5)	2	3	(0.3)	3
Osteoarthritis	1	(0.1)	1	2	(0.5)	2	3	(0.3)	3
Arthralgia	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Arthritis	1	(0.1)	1	0		0	1	(0.1)	1
Bursitis	0		0	1	(0.3)	1	1	(0.1)	1
Musculoskeletal pain	1	(0.1)	1	0		0	1	(0.1)	1
Neck pain	0		0	1	(0.3)	1	1	(0.1)	1
Osteitis	1	(0.1)	1	0		0	1	(0.1)	1
Pain in extremity	1	(0.1)	1	0		0	1	(0.1)	1
Pathological fracture	0		0	1	(0.3)	1	1	(0.1)	1
Periarthritis	0		0	1	(0.3)	1	1	(0.1)	1
Spinal pain	1	(0.1)	1	0		0	1	(0.1)	1
Metabolism and nutrition disorders	13	(1.7)	14	7	(1.8)	7	20	(1.8)	21
Dehydration	6	(0.8)	6	4	(1.1)	4	10	(0.9)	10
Hyponatraemia	4	(0.5)	4	0		0	4	(0.4)	4
Diabetic metabolic decompensation	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2

SOTIO: SP005/CIL-RA/FINAL/AECLXRP.SAS

Produced: 19 June 2020, 11:41

Page 11 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Metabolism and nutrition disorders (cont.)									
Decreased appetite	1	(0.1)	1	0			1	(0.1)	1
Diabetes mellitus	1	(0.1)	1	0			1	(0.1)	1
Failure to thrive	0			1	(0.3)	1	1	(0.1)	1
Hyperglycaemia	0			1	(0.3)	1	1	(0.1)	1
Hypoglycaemia	1	(0.1)	1	0			1	(0.1)	1
Injury, poisoning and procedural complications									
Subdural haematoma	13	(1.7)	15	6	(1.6)	6	19	(1.7)	21
Ankle fracture	2	(0.3)	2	1	(0.3)	1	3	(0.3)	3
Hip fracture	0			2	(0.5)	2	2	(0.2)	2
Lower limb fracture	2	(0.3)	2	0			2	(0.2)	2
Spinal compression fracture	2	(0.3)	2	0			2	(0.2)	2
Cystitis radiation	0			2	(0.5)	2	2	(0.2)	2
Femoral neck fracture	1	(0.1)	1	0			1	(0.1)	1
Fibula fracture	1	(0.1)	1	0			1	(0.1)	1
Gastrointestinal stoma complication	0			1	(0.3)	1	1	(0.1)	1
Jaw fracture	1	(0.1)	1	0			1	(0.1)	1
Lumbar vertebral fracture	1	(0.1)	1	0			1	(0.1)	1
Postoperative wound complication	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AECLXRP.SAS

Produced: 19 June 2020, 11:41

Page 12 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Injury, poisoning and procedural complications (cont.)									
Radiation proctitis	1	(0.1)	1	0			1	(0.1)	1
Skull fracture	1	(0.1)	1	0			1	(0.1)	1
Subdural haemorrhage	1	(0.1)	1	0			1	(0.1)	1
Vascular disorders									
Deep vein thrombosis	4	(0.5)	5	1	(0.3)	1	5	(0.4)	6
Hypotension	2	(0.3)	2	0			2	(0.2)	2
Shock	2	(0.3)	2	0			2	(0.2)	2
Aortic stenosis	1	(0.1)	1	0			1	(0.1)	1
Hypertension	0			1	(0.3)	1	1	(0.1)	1
Hypovolaemic shock	1	(0.1)	1	0			1	(0.1)	1
Temporal arteritis	1	(0.1)	1	0			1	(0.1)	1
Thrombophlebitis	0			1	(0.3)	1	1	(0.1)	1
Venous thrombosis limb	0			1	(0.3)	1	1	(0.1)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
Cancer pain	1	(0.1)	1	3	(0.8)	3	4	(0.4)	4
Basal cell carcinoma	2	(0.3)	2	0			2	(0.2)	2
Malignant melanoma	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 13 of 16

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Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (cont.)									
Adenocarcinoma of colon	1	(0.1)	1	0			1	(0.1)	1
Anal squamous cell carcinoma	1	(0.1)	1	0			1	(0.1)	1
Carcinoid tumour	1	(0.1)	1	0			1	(0.1)	1
Cardiac myxoma	1	(0.1)	1	0			1	(0.1)	1
Chondrosarcoma	0			1	(0.3)	1	1	(0.1)	1
Chronic lymphocytic leukaemia	1	(0.1)	1	0			1	(0.1)	1
Malignant pleural effusion	1	(0.1)	1	0			1	(0.1)	1
Eye disorders									
Diplopia	3	(0.4)	3	0			3	(0.3)	3
Retinal detachment	1	(0.1)	1	0			1	(0.1)	1
Uveitis	1	(0.1)	1	0			1	(0.1)	1
Immune system disorders									
Allergy to arthropod sting	2	(0.3)	2	1	(0.3)	1	3	(0.3)	3
Anaphylactic reaction	1	(0.1)	1	0			1	(0.1)	1
Hypersensitivity	1	(0.1)	1	0			1	(0.1)	1
	0			1	(0.3)	1	1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 14 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Investigations	1	(0.1)	1	2	(0.5)	2	3	(0.3)	3
Blood creatinine increased	1	(0.1)	1	0			1	(0.1)	1
Computerised tomogram abnormal	0			1	(0.3)	1	1	(0.1)	1
Neutrophil count decreased	0			1	(0.3)	1	1	(0.1)	1
Hepatobiliary disorders	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Hepatic cyst	0			1	(0.3)	1	1	(0.1)	1
Hepatic failure	1	(0.1)	1	0			1	(0.1)	1
Psychiatric disorders	2	(0.3)	2	0			2	(0.2)	2
Mental status changes	1	(0.1)	1	0			1	(0.1)	1
Nightmare	1	(0.1)	1	0			1	(0.1)	1
Reproductive system and breast disorders	2	(0.3)	2	0			2	(0.2)	2
Pelvic pain	1	(0.1)	1	0			1	(0.1)	1
Scrotal oedema	1	(0.1)	1	0			1	(0.1)	1
Product issues	1	(0.1)	2	0			1	(0.1)	2
Device occlusion	1	(0.1)	2	0			1	(0.1)	2

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 15 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 2 Serious Treatment Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Ear and labyrinth disorders	1	(0.1)	1	0		0	1	(0.1)	1
Vertigo	1	(0.1)	1	0		0	1	(0.1)	1
Skin and subcutaneous tissue disorders	1	(0.1)	1	0		0	1	(0.1)	1
Rash erythematous	1	(0.1)	1	0		0	1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AECLXRP.SAS

Produced: 19 June 2020, 11:41

Page 16 of 16

Source: Listing 16.2.7.4 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 3 Fatal Adverse Treatment Emergent Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Any AE	39	(5.2)	42	30	(7.9)	31	69	(6.1)	73
General disorders and administration site conditions	15	(2.0)	15	15	(4.0)	15	30	(2.7)	30
General physical health deterioration	7	(0.9)	7	8	(2.1)	8	15	(1.3)	15
Death	5	(0.7)	5	5	(1.3)	5	10	(0.9)	10
Disease progression	2	(0.3)	2	1	(0.3)	1	3	(0.3)	3
Multiple organ dysfunction syndrome	0			1	(0.3)	1	1	(0.1)	1
Sudden death	1	(0.1)	1	0			1	(0.1)	1
Infections and infestations	5	(0.7)	5	5	(1.3)	5	10	(0.9)	10
Pneumonia	3	(0.4)	3	2	(0.5)	2	5	(0.4)	5
Sepsis	2	(0.3)	2	1	(0.3)	1	3	(0.3)	3
Neutropenic sepsis	0			1	(0.3)	1	1	(0.1)	1
Pyelonephritis	0			1	(0.3)	1	1	(0.1)	1
Respiratory, thoracic and mediastinal disorders	8	(1.1)	8	2	(0.5)	2	10	(0.9)	10
Acute respiratory failure	3	(0.4)	3	1	(0.3)	1	4	(0.4)	4
Pulmonary embolism	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Acute respiratory distress syndrome	1	(0.1)	1	0			1	(0.1)	1
Hydrothorax	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 1 of 3

Source: Listing 14.3.2.1 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

Raw Data Export: 04DEC2019 External Data: Labcorp: 04DEC2019 Bioclinica: 22NOV2019 IVRS: 17DEC2019

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AE Table 3 Fatal Adverse Treatment Emergent Events by System Organ Class and Preferred Term
(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)		Placebo+ Chemotherapy (N=379)		Overall (N=1128)	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders (cont.)						
Interstitial lung disease	1	(0.1)	0		1	(0.1)
Respiratory failure	1	(0.1)	0		1	(0.1)
Cardiac disorders	3	(0.4)	5	(1.3)	8	(0.7)
Myocardial infarction	3	(0.4)	1	(0.3)	4	(0.4)
Cardiac arrest	0		2	(0.5)	2	(0.2)
Acute myocardial infarction	0		1	(0.3)	1	(0.1)
Cardiomyopathy	0		1	(0.3)	1	(0.1)
Nervous system disorders	2	(0.3)	1	(0.3)	3	(0.3)
Cerebral haemorrhage	1	(0.1)	0		1	(0.1)
Cerebrovascular accident	1	(0.1)	0		1	(0.1)
Diabetic coma	0		1	(0.3)	1	(0.1)
Hepatobiliary disorders	2	(0.3)	0		2	(0.2)
Hepatic failure	2	(0.3)	0		2	(0.2)
Injury, poisoning and procedural complications	0		2	(0.5)	2	(0.2)
Subdural haematoma	0		2	(0.5)	2	(0.2)

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 2 of 3

Source: Listing 14.3.2.1 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

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(Safety Population)

System Organ Class Preferred Term	DCVAC/PCa+ Chemotherapy (N=749)			Placebo+ Chemotherapy (N=379)			Overall (N=1128)		
	n	(%)	E	n	(%)	E	n	(%)	E
Metabolism and nutrition disorders	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Cachexia	1	(0.1)	1	1	(0.3)	1	2	(0.2)	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	(0.3)	2	0			2	(0.2)	2
Anal squamous cell carcinoma	1	(0.1)	1	0			1	(0.1)	1
Malignant pleural effusion	1	(0.1)	1	0			1	(0.1)	1
Vascular disorders	2	(0.3)	2	0			2	(0.2)	2
Shock	2	(0.3)	2	0			2	(0.2)	2
Gastrointestinal disorders	1	(0.1)	1	0			1	(0.1)	1
Gastrointestinal haemorrhage	1	(0.1)	1	0			1	(0.1)	1
Renal and urinary disorders	1	(0.1)	1	0			1	(0.1)	1
Renal failure	1	(0.1)	1	0			1	(0.1)	1

SOTIO: SP005/CIL-RA/FINAL/AEC1XRP.SAS

Produced: 19 June 2020, 11:41

Page 3 of 3

Source: Listing 14.3.2.1 - Source Data: ADAE.sas7bdat - 19JUN2020 7:17, ADSL.sas7bdat - 19JUN2020 7:17

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