Clinical trial results:
Randomized, open-label, parallel-group, multi-centre phase II clinical trial with active cellular immunotherapy DCVAC/PCa in patients with localized high-risk prostate cancer after primary radiotherapy

Summary

EudraCT number	2011-004967-65
Trial protocol	CZ
Global end of trial date	11 October 2018

Results information

Result version number	v1 (current)
This version publication date	23 October 2019
First version publication date	23 October 2019

Trial information

Trial identification

Sponsor protocol code	SP004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02107430
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2018
Global end of trial reached?	Yes
Global end of trial date	11 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of study SP004 was to estimate the survival rate of patients without prostate-specific antigen (PSA) failure, the survival rate of patients without initiation of salvage therapy 5 years after randomization, time to objective disease progression, overall survival (OS), and the incidence of adverse events (AEs).

Protection of trial subjects:

Not applicable

Background therapy:

Both treatment groups started radiotherapy 4 weeks (±1 week) after randomization. A minimum dose of 44 Gy targeted at the small pelvis (22 fractions delivered over 4 weeks + 2 days or a biologically equivalent dose) and a minimum dose of 74 Gy at the prostate ± seminal vesicles (37 fractions delivered over 7 weeks + 2 days or a biologically equivalent dose) were administered.

Both treatment groups continued neoadjuvant androgen deprivation therapy (ADT) with luteinizing hormone-releasing hormone (LHRH) analogs during radiotherapy and started adjuvant ADT with LHRH analogs or bicalutamide within 1 week after the end of radiotherapy. Adjuvant ADT continued for at least 2 years.

Evidence for comparator:

Not applicable

Actual start date of recruitment	28 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	16
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Nine clinical study sites in the Czech Republic participated in the study, and 6 screened at least 1 patient. Recruitment started on 28-Mar-2012 (first patient signed the informed consent form).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Immuno-therapy group

Arm description:

DCVAC/PCa combined with radiotherapy and ADT; patients in the immunotherapy group were treated with 50 mg/day of oral cyclophosphamide for 7 days before the first dose of DCVAC/PCa and applied imiquimod cream to the planned DCVAC/PCa injection sites 24 hours before each DCVAC/PCa administration

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

Dosage and administration details:

Subcutaneous injection of approximately 1×10e7 autologous dendritic cells; oral cyclophosphamide 50 mg/day for 7 days before the first dose of DCVAC/PCa; imiquimod cream applied to the planned DCVAC/PCa injection sites 24 hours before each DCVAC/PCa administration

Arm title	Control group

Arm description:

Radiotherapy and ADT alone

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Immuno-therapy group	Control group
Started	31	31
Completed	22	17
Not completed	9	14
End of study visit earlier than per Protocol	1	-
Consent withdrawn by subject	4	5
Physician decision	1	1
Adverse event, non-fatal	-	3

Reason not available	-	1
Death	3	1
Protocol deviation	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Immuno-therapy group
Reporting group description:	
DCVAC/PCa combined with radiotherapy and ADT; patients in the immunotherapy group were treated with 50 mg/day of oral cyclophosphamide for 7 days before the first dose of DCVAC/PCa and applied imiquimod cream to the planned DCVAC/PCa injection sites 24 hours before each DCVAC/PCa administration	
Reporting group title	Control group
Reporting group description:	
Radiotherapy and ADT alone	

Reporting group values	Immuno-therapy group	Control group	Total
Number of subjects	31	31	62
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	10	6	16
From 65-84 years	21	25	46
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	0	0
Male	31	31	62

End points

End points reporting groups

Reporting group title	Immuno-therapy group

Reporting group description:

DCVAC/PCa combined with radiotherapy and ADT; patients in the immunotherapy group were treated with 50 mg/day of oral cyclophosphamide for 7 days before the first dose of DCVAC/PCa and applied imiquimod cream to the planned DCVAC/PCa injection sites 24 hours before each DCVAC/PCa administration

Reporting group title	Control group

Reporting group description:

Radiotherapy and ADT alone

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

Subject analysis set description:

The Intention-to-treat (ITT) population consisted of all randomized patients except those for whom no data were available following the Randomization visit. More precisely, patients who did not have any post-randomization visit and any data regarding survival follow-up were excluded from the ITT population.

Subject analysis set title	Per Protocol set
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol set (PPS) was defined as a subset of the ITT population from which all patients with a significant protocol deviation were excluded. The following was considered as a significant protocol deviation: i) Not meeting 1 or more inclusion criteria; ii) Meeting 1 or more exclusion criteria; iii) Treatment assignment error; iv) Use of prohibited concomitant medication; v) Serious non-compliance with treatment regimen; vi) Missed essential assessment. Patients who were randomized to the immunotherapy group and did not receive any dose of DCVAC/PCa for any reason (including leukapheresis or production failure) were not included in the PPS. In the same manner, patients who were randomized to the control group but discontinued before or at Visit 1 were not included in the PPS. Patients who did not undergo radiotherapy/ were not using appropriate ADT or used a prohibited concomitant medication were not included in the PPS.

Primary: Proportion of patients alive who were without PSA failure at 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy group - 26 patients, control group - 23 patients)

End point title	Proportion of patients alive who were without PSA failure at 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy group - 26 patients, control group - 23 patients)

End point description:

End point type	Primary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26[1]	23[2]		
Units: Patients	18	15		

Notes:
[1] - Patients alive 5 years after randomization
[2] - Patients alive 5 years after randomization

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Primary: Proportion of patients alive who were without PSA failure at 5 years after randomization, ITT population (all patients)

End point title	Proportion of patients alive who were without PSA failure at 5 years after randomization, ITT population (all patients)

End point description:

End point type	Primary

End point timeframe:
From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Patients	18	15		

Statistical analyses

Statistical analysis title	Primary
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6111
Method	Fisher exact

Primary: Time to PSA failure, ITT population (main analysis)	
End point title	Time to PSA failure, ITT population (main analysis)
End point description:	
End point type	Primary
End point timeframe:	
From randomization to 5 years after randomization	

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	43.58 (± 1.664)	53.44 (± 1.836)		

Statistical analyses

Statistical analysis title	Main analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6847
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.733
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.164
upper limit	3.278

Secondary: Time to PSA failure, ITT population (sensitivity analysis A)	
End point title	Time to PSA failure, ITT population (sensitivity analysis A)
End point description:	
Sensitivity analysis A: An analysis using the ITT population based on data until the End of study visit only	
End point type	Secondary
End point timeframe:	
From randomization to 5 years after randomization	

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	43.51 (± 1.721)	49.56 (± 1.853)		

Statistical analyses

Statistical analysis title	Sensitivity analysis A
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9588
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.959
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.193
upper limit	4.751

Secondary: Time to PSA failure, ITT population (sensitivity analysis B)

End point title	Time to PSA failure, ITT population (sensitivity analysis B)

End point description:

Sensitivity analysis B: An analysis using the ITT population in which data from patients using adjuvant ADT for less than 2 years were used only until the end of ADT + 3 months

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	43.58 (± 1.664)	53.28 (± 1.894)		

Statistical analyses

Statistical analysis title	Sensitivity analysis B
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6792
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.729
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.163
upper limit	3.26

Secondary: Time to PSA failure, PPS (sensitivity analysis C)	
End point title	Time to PSA failure, PPS (sensitivity analysis C)
End point description: Sensitivity analysis C: An analysis using the PPS	
End point type	Secondary
End point timeframe: From randomization to 5 years after randomization	

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	11		
Units: month				
arithmetic mean (standard error)	12.49 (± 1000000)	1000000 (± 1000000)		

Statistical analyses

Statistical analysis title	Sensitivity analysis C
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9985
Method	Regression, Cox

Secondary: Proportion of patients without salvage therapy 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy group - 26 patients, control group - 23 patients)

End point title	Proportion of patients without salvage therapy 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy group - 26 patients, control group - 23 patients)

End point description:

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26[3]	23[4]		
Units: Patients	18	15		

Notes:

[3] - Patients alive 5 years after randomization

[4] - Patients alive 5 years after randomization

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Proportion of patients without salvage therapy 5 years after randomization, ITT population (all patients)

End point title	Proportion of patients without salvage therapy 5 years after randomization, ITT population (all patients)

End point description:

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Patients	18	15		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6111
Method	Fisher exact

Secondary: Time to initiation of salvage therapy, ITT population (main analysis)

End point title	Time to initiation of salvage therapy, ITT population (main analysis)

End point description:

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: months				
arithmetic mean (standard error)	48.42 (± 0.102)	54.21 (± 1.784)		

Statistical analyses

Statistical analysis title	Main analysis
Comparison groups	Immuno-therapy group v Control group

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6429
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.655
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.109
upper limit	3.92

Secondary: Time to initiation of salvage therapy, ITT population (sensitivity analysis A)

End point title	Time to initiation of salvage therapy, ITT population (sensitivity analysis A)
End point description:	
Sensitivity analysis A: An analysis using the ITT population based on data until the End of study visit only	
End point type	Secondary
End point timeframe:	
From randomization to 5 years after randomization	

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	48.42 (± 0.102)	54.09 (± 1.913)		

Statistical analyses

Statistical analysis title	Sensitivity analysis A
Comparison groups	Control group v Immuno-therapy group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5933
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.614

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.103
upper limit	3.677

Secondary: Time to initiation of salvage therapy, ITT population (sensitivity analysis B)

End point title	Time to initiation of salvage therapy, ITT population (sensitivity analysis B)

End point description:

Sensitivity analysis B: An analysis using the ITT population in which data from patients using adjuvant ADT for less than 2 years were used only until the end of ADT + 3 months

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	48.40 (± 0.122)	54.20 (± 1.784)		

Statistical analyses

Statistical analysis title	Sensitivity analysis B
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6398
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.652
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.109
upper limit	3.904

Secondary: Time to initiation of salvage therapy, PPS (sensitivity analysis C)

End point title	Time to initiation of salvage therapy, PPS (sensitivity analysis C)

End point description:

Sensitivity analysis C: An analysis using the PPS

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	11		
Units: month				
arithmetic mean (standard error)	1000000 (± 1000000)	1000000 (± 1000000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy group - 26 patients, control group - 23 patients) – approach A

End point title	Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy group - 26 patients, control group - 23 patients) – approach A

End point description:

Approach A: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease.

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26[5]	23[6]		
Units: Patients	20	16		

Notes:

[5] - Patients alive 5 years after randomization

[6] - Patients alive 5 years after randomization

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7471
Method	Fisher exact

Secondary: Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (all patients) – approach A

End point title	Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (all patients) – approach A

End point description:

Approach A: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease.

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Patients	20	16		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Control group v Immuno-therapy group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4404
Method	Fisher exact

Secondary: Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy group - 26 patients, control group - 23 patients) – approach B

End point title	Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (patients alive 5 years after randomization: immunotherapy

	group - 26 patients, control group - 23 patients) – approach B

End point description:

Approach B: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease, and for whom an objective tumor assessment was missed but there is a reliable evidence of stable disease based on PSA values measured regularly as per the Protocol schedule until 5 years after randomization (i.e., no PSA failure was observed).

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26[7]	23[8]		
Units: Patients	21	17		

Notes:

[7] - Patients alive 5 years after randomization

[8] - Patients alive 5 years after randomization

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7341
Method	Fisher exact

Secondary: Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (all patients) – approach B

End point title	Proportion of patients alive who were without objective disease progression at 5 years after randomization, ITT population (all patients) – approach B

End point description:

Approach B: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease, and for whom an objective tumor assessment was missed but there is a reliable evidence of stable disease based on PSA values measured regularly as per the Protocol schedule until 5 years after randomization (i.e., no PSA failure was observed).

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Patients	21	17		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4345
Method	Fisher exact

Secondary: Time to objective disease progression, ITT population (main analysis) – approach A

End point title	Time to objective disease progression, ITT population (main analysis) – approach A

End point description:

Approach A: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease.

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	44.14 (± 2.443)	51.57 (± 2.211)		

Statistical analyses

Statistical analysis title	Main analysis
Comparison groups	Immuno-therapy group v Control group

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9967
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.363
upper limit	2.764

Secondary: Time to objective disease progression, ITT population (main analysis) – approach B

End point title	Time to objective disease progression, ITT population (main analysis) – approach B

End point description:

Approach B: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease, and for whom an objective tumor assessment was missed but there is a reliable evidence of stable disease based on PSA values measured regularly as per the Protocol schedule until 5 years after randomization (i.e., no PSA failure was observed).

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	44.32 (± 2.369)	52.02 (± 1.984)		

Statistical analyses

Statistical analysis title	Main analysis
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.895
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.071

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.388
upper limit	2.954

Secondary: Time to objective disease progression, ITT population (sensitivity analysis B) – approach A

End point title	Time to objective disease progression, ITT population (sensitivity analysis B) – approach A

End point description:

Sensitivity analysis B: An analysis using the ITT population in which data from patients using adjuvant ADT for less than 2 years were to be used only until the end of ADT + 3 months
Approach A: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	43.50 (± 2.692)	50.73 (± 2.606)		

Statistical analyses

Statistical analysis title	Sensitivity analysis B
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8788
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.924
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.335
upper limit	2.549

Secondary: Time to objective disease progression, ITT population (sensitivity analysis B) – approach B

End point title	Time to objective disease progression, ITT population (sensitivity analysis B) – approach B

End point description:

Sensitivity analysis B: Analysis using the ITT population in which data from patients using adjuvant ADT for less than 2 years were to be used only until the end of ADT + 3 months
Approach B: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease, and for whom an objective tumor assessment was missed but there is a reliable evidence of stable disease based on PSA values measured regularly as per the Protocol schedule until 5 years after randomization (i.e., no PSA failure was observed)

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	44.13 (± 2.410)	51.62 (± 2.092)		

Statistical analyses

Statistical analysis title	Sensitivity analysis B
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9078
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.062
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.385
upper limit	2.93

Secondary: Time to objective disease progression, PPS (sensitivity analysis C) – approach A

End point title	Time to objective disease progression, PPS (sensitivity analysis C) – approach A

End point description:

Sensitivity analysis C: An analysis using the PPS

Approach A: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	11		
Units: month				
arithmetic mean (standard error)	28.20 (± 1.167)	44.31 (± 0.290)		

Statistical analyses

Statistical analysis title	Sensitivity analysis C
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5886
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.582
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.082
upper limit	4.135

Secondary: Time to objective disease progression, PPS (sensitivity analysis C) – approach B

End point title	Time to objective disease progression, PPS (sensitivity analysis C) – approach B

End point description:

Sensitivity analysis C: An analysis using the PPS
Approach B: Disease progression-free patients were those for whom an objective tumor assessment (CT scan and scintigraphy) 5 years after randomization shows evidence of NON-progressive disease, and for whom an objective tumor assessment was missed but there is a reliable evidence of stable disease based on PSA values measured regularly as per the Protocol schedule until 5 years after randomization (i.e., no PSA failure was observed)

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	11		
Units: month				
arithmetic mean (standard error)	28.20 (± 1.167)	44.33 (± 0.265)		

Statistical analyses

Statistical analysis title	Sensitivity analysis C
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6578
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.642
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	4.56

Secondary: Proportion of patients who were alive 5 years after randomization, overall survival, ITT population

End point title	Proportion of patients who were alive 5 years after randomization, overall survival, ITT population

End point description:

End point type	Secondary

End point timeframe:

From randomization to 5 years after randomization

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Patients	26	23		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Control group v Immuno-therapy group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5339
Method	Fisher exact

Secondary: Overall survival, ITT population

End point title	Overall survival, ITT population

End point description:

End point type	Secondary

End point timeframe:

From randomization to the end of the study

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	45.90 (± 2.065)	47.85 (± 1.036)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Immuno-therapy group v Control group

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9711
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.023
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.296
upper limit	3.536

Secondary: Overall survival, ITT population (sensitivity analysis B)

End point title	Overall survival, ITT population (sensitivity analysis B)

End point description:

Sensitivity analysis B: An analysis using the ITT population in which data from patients using adjuvant ADT for less than 2 years were to be used only until the end of ADT + 3 months

End point type	Secondary

End point timeframe:

From randomization to the end of the study

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: month				
arithmetic mean (standard error)	45.74 (± 2.116)	47.64 (± 1.142)		

Statistical analyses

Statistical analysis title	Sensitivity analysis B
Comparison groups	Control group v Immuno-therapy group
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9547
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.037

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	3.583

Secondary: Overall survival, PPS (sensitivity analysis C)

End point title	Overall survival, PPS (sensitivity analysis C)
End point description:	
Sensitivity analysis C: An analysis using the PPS	
End point type	Secondary
End point timeframe:	
From randomization to the end of the study	

End point values	Immuno-therapy group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	11		
Units: month				
arithmetic mean (standard error)	28.25 (± 1.107)	44.33 (± 0.265)		

Statistical analyses

Statistical analysis title	Sensitivity analysis C
Comparison groups	Immuno-therapy group v Control group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6163
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.606
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.085
upper limit	4.302

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs): from Visit 1 (start of DCVAC/PCa in the immunotherapy group) to 30 days after Visit 10/ the End of treatment visit (30 days after the last dose of DCVAC/PCa in the immunotherapy group). Deaths: from consent signature to study end

Adverse event reporting additional description:

Only treatment-emergent AEs (TEAEs) were analyzed. The tables include information on TEAEs, serious TEAEs, and all deaths. Causality was assessed by investigators. A suspected unexpected serious adverse reaction (lymphedema) was reported in one patient.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	Immuno-therapy group
Reporting group description: -	
Reporting group title	Control group

Reporting group description: -

Serious adverse events	Immuno-therapy group	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)	4 / 29 (13.79%)	
number of deaths (all causes)	5	5	
number of deaths resulting from adverse events	1	0	
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiogenic shock			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urethral obstruction			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Immuno-therapy group	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 30 (93.33%)	29 / 29 (100.00%)	
Investigations			

Weight decreased			
subjects affected / exposed	1 / 30 (3.33%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Weight increased			
subjects affected / exposed	1 / 30 (3.33%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Injury, poisoning and procedural complications			
Cystitis radiation			
subjects affected / exposed	3 / 30 (10.00%)	5 / 29 (17.24%)	
occurrences (all)	3	5	
Gastroenteritis radiation			
subjects affected / exposed	3 / 30 (10.00%)	5 / 29 (17.24%)	
occurrences (all)	3	5	
Radiation proctitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Radiation sickness syndrome			
subjects affected / exposed	0 / 30 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	3	
Vascular disorders			
Hot flush			
subjects affected / exposed	3 / 30 (10.00%)	0 / 29 (0.00%)	
occurrences (all)	3	0	
Hypertension			
subjects affected / exposed	2 / 30 (6.67%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Atrial fibrillation			
subjects affected / exposed	2 / 30 (6.67%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	2 / 30 (6.67%)	6 / 29 (20.69%)	
occurrences (all)	2	6	
Oedema peripheral			
subjects affected / exposed	5 / 30 (16.67%)	2 / 29 (6.90%)	
occurrences (all)	5	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	1 / 30 (3.33%)	7 / 29 (24.14%)	
occurrences (all)	1	7	
Faeces soft			
subjects affected / exposed	2 / 30 (6.67%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	2 / 30 (6.67%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Gynaecomastia			
subjects affected / exposed	5 / 30 (16.67%)	7 / 29 (24.14%)	
occurrences (all)	5	7	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Skin burning sensation			
subjects affected / exposed	3 / 30 (10.00%)	0 / 29 (0.00%)	
occurrences (all)	3	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 30 (3.33%)	4 / 29 (13.79%)	
occurrences (all)	1	4	
Nocturia			
subjects affected / exposed	5 / 30 (16.67%)	3 / 29 (10.34%)	
occurrences (all)	5	3	

Renal failure			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Urinary retention			
subjects affected / exposed	2 / 30 (6.67%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 30 (6.67%)	4 / 29 (13.79%)	
occurrences (all)	2	4	
Back pain			
subjects affected / exposed	0 / 30 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	3	
Joint swelling			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	4 / 29 (13.79%)	
occurrences (all)	0	4	
Infections and infestations			
Epididymitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Influenza			
subjects affected / exposed	0 / 30 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	3	
Urinary tract infection			
subjects affected / exposed	2 / 30 (6.67%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Viral infection			
subjects affected / exposed	2 / 30 (6.67%)	3 / 29 (10.34%)	
occurrences (all)	2	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 30 (3.33%)	2 / 29 (6.90%)	
occurrences (all)	1	2	

Diabetes mellitus			
subjects affected / exposed	0 / 30 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Hyperglycaemia			
subjects affected / exposed	2 / 30 (6.67%)	2 / 29 (6.90%)	
occurrences (all)	2	2	
Hypokalaemia			
subjects affected / exposed	2 / 30 (6.67%)	5 / 29 (17.24%)	
occurrences (all)	2	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2011	- European Pharminvent Services to be responsible for pharmacovigilance services - Added specification of assessment for leukapheresis technical feasibility (vein access evaluation) prior the procedure for patients in immunotherapy group - Specification for HIV tests was added (CE marked kits; accredited laboratory) - Updated exclusion criteria to rule out patients indicated for chemotherapy (docetaxel and prednisone)
05 March 2012	- Updated visit schedule to clarify how active cellular immunotherapy will be applied in connection with RT - Updated SAE reporting - Exclusion criterion E9 was updated to be more general - Updated information on ADT dosing - Updated sampling period for Immunology and Immunomonitoring - Clarification of cyclophosphamide dosing - Details provided about CT/scintigraphy readings - Added criteria for early patient termination in the study - Active cellular immunotherapy transport and application description updated - PSA Failure terminology update
13 December 2012	- Updated instruction for ADT during RT based on 2012 European Association of Urology Guidelines on Prostate Cancer)
11 June 2015	- Detailed description of exploratory objectives, endpoints and analysis - Clearly distinguishing IMP from stimulating medication - Detailed description of laboratory testing performed, including samples for research - Statistical analysis section updated - Information about phase I/II clinical trials conducted by University Hospital in Motol updated per current knowledge - Section on concomitant medication was updated - Updated safety reporting sections, including the transfer of safety monitoring responsibilities from European Pharminvent Services to SOTIO a.s. - New term introduction: EoT, EoS, EoS Examination visit, Follow-up and Survival Follow-up - Updated section Rationale for Prostate Cancer Immunotherapy - Terminology harmonization
29 May 2018	- Adding collection of data of PSA levels and salvage therapy in the survival follow-up - Signature page according to new Standard Operating Procedure

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported