Clinical trial results:
Open-label, one-arm, multi-centre phase II clinical trial with second cycle of active cellular immunotherapy DCVAC/PCa in patients with localized prostate cancer after primary radical prostatectomy and without objective progression on the first cycle of DCVAC/PCa

Summary

EudraCT number	2013-003809-26
Trial protocol	CZ
Global end of trial date	20 March 2017

Results information

Result version number	v1 (current)
This version publication date	01 April 2018
First version publication date	01 April 2018

Trial information

Trial identification

Sponsor protocol code	SP010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02137746
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sotio a.s.
Sponsor organisation address	Jankovcova 1518/2, Prague, Czech Republic, 170 00
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	20 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2017
Global end of trial reached?	Yes
Global end of trial date	20 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study SP010 was to establish the safety profile of extended application of active cellular immunotherapy prepared from repeated leukapheresis. The safety of the second cycle of active cellular immunotherapy involving the second leukapheresis procedure was to be assessed in patients who successfully received all doses of active cellular immunotherapy after RPE or salvage radiotherapy and who were without objective progression of the disease during the study SP003. Other objectives were to evaluate prostate-specific antigen (PSA) doubling time (DT) in the treatment phase of the study SP010 and to compare it with PSADT in the study SP003; to evaluate PSADT in the follow-up phase of the study SP010; to determine the proportion of patients who had progressive increase in PSA, objective disease progression, or further anticancer therapy within 2 years of enrollment; and to evaluate overall survival (OS).

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 December 2013
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: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	9
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eight clinical study centers in the Czech Republic participated in the study SP010 and all recruited (screened) at least 1 patient. Recruitment started on 17-Dec-2013 (first patient signed the informed consent form) and ended on 02-Apr-2015 (last patient signed the informed consent form).

Pre-assignment

Screening details:

Screened: 24
Enrolled: 23
Analyzed for efficacy: 23
Analyzed for safety: 23

Period 1

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

Arms

Arm title	Immunotherapy group

Arm description:

DCVAC/PCa

Arm type	Experimental
Investigational medicinal product name	Overall trial (overall period)
Investigational medicinal product code	Not applicable
Other name	Not applicable
Pharmaceutical forms	Dispersion for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection of approximately 1×10e7 autologous DCs

Number of subjects in period 1	Immunotherapy group
Started	23
Completed	23

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	23	23	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	66.26		
full range (min-max)	54.08 to 74.24	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	23	23	

End points

End points reporting groups

Reporting group title	Immunotherapy group
Reporting group description: DCVAC/PCa	
Subject analysis set title	ITT-derived populations
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The ITT population consisted of all enrolled patients except those for whom no data were available following the baseline visit. For endpoints where PSADT was the main interest, only patients who had 2 or more PSA values in the examined time period were taken into consideration. It means that for the treatment phase, the ITT population with 2 or more PSA values in the treatment phase (ITT2t) was examined. The same applied to the follow-up phase with the population ITT2f.

Primary: Incidence of AEs, SAEs, clinically significant laboratory abnormalities, and changes in vital signs

End point title	Incidence of AEs, SAEs, clinically significant laboratory abnormalities, and changes in vital signs[1]

End point description:

Please see the sention on adverse events

End point type	Primary

End point timeframe:

Duration of the study

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal analysis was done for the primary end point of this single-arm study. See also the section on adverse events.

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Not applicable	0			

Statistical analyses

No statistical analyses for this end point

Secondary: PSADT in the treatment phase

End point title	PSADT in the treatment phase

End point description:

End point type	Secondary

End point timeframe:

From Dose 1 to Dose 10

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	23[2]			
Units: Months				
median (full range (min-max))	21.19 (3.52 to 100)			

Notes:

[2] - ITT2t

Statistical analyses

No statistical analyses for this end point

Secondary: Comparing PSADT measured in the treatment phase of the study SP010 with PSADT measured in the study SP003

End point title	Comparing PSADT measured in the treatment phase of the study SP010 with PSADT measured in the study SP003

End point description:

Differences between PSADT in the study SP003 and PSADT in the study SP010

End point type	Secondary

End point timeframe:

Treatment phase of the studies SP003 and SP010

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	23[3]			
Units: Month				
median (full range (min-max))	7.39 (-96.48 to 85.87)			

Notes:

[3] - ITT2t

Statistical analyses

No statistical analyses for this end point

Secondary: PSADT in the follow-up phase

End point title	PSADT in the follow-up phase

End point description:

End point type	Secondary

End point timeframe:

From the completed V10 to 2 years from enrollment in the study

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	22[4]			
Units: Months				
median (full range (min-max))	15.73 (6.72 to 100)			

Notes:

[4] - ITT2f

Statistical analyses

No statistical analyses for this end point

Secondary: Comparing PSADT measured in the follow-up phase with PSADT in the treatment phase

End point title	Comparing PSADT measured in the follow-up phase with PSADT in the treatment phase

End point description:

Differences between PSADT in the treatment phase and PSADT in the follow-up phase

End point type	Secondary

End point timeframe:

From V1 to 2 years from enrollment in the study

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	22[5]			
Units: Months				
median (full range (min-max))	-2.74 (-93.28 to 96.48)			

Notes:

[5] - ITT2f

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients who required any further anticancer therapy

End point title	Proportion of patients who required any further anticancer therapy

End point description:

End point type	Secondary

End point timeframe:

Within 2 years from enrollment in the study

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	23[6]			
Units: Proportion of pts with further therapy				
number (confidence interval 95%)	0.0870 (0.0107 to 0.2804)			

Notes:

[6] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients who had progressive increase in PSA

End point title	Proportion of patients who had progressive increase in PSA

End point description:

End point type	Secondary

End point timeframe:

Within 2 years from enrollment in the study

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	11[7]			
Units: Proportion of pts with progressive PSA				
number (confidence interval 95%)	0.182 (0.029 to 0.442)			

Notes:

[7] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

2 years after enrollment

End point values	Immunotherapy group			
Subject group type	Reporting group			
Number of subjects analysed	23[8]			
Units: Proportion of pts alive				
number (confidence interval 95%)	1.000 (1.000 to 1.000)			

Notes:

[8] - ITT

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent AEs and SAEs: from V1 to 30 days after the last dose of DCVAC/PCa
Deaths: from consent signature to trial termination

Adverse event reporting additional description:

The tables include information on treatment-emergent AEs and treatment-emergent SAEs. An event causally related to treatment was one which was assessed by investigators as causally related to DCVAC/PCa administration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Immunotherapy group

Reporting group description:

DCVAC/PCa

Serious adverse events	Immunotherapy group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 23 (8.70%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Immunotherapy group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 23 (21.74%)		
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Renal and urinary disorders			

Renal colic subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all)	 1 / 23 (4.35%) 1 1 / 23 (4.35%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 1 / 23 (4.35%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2013	- Update of the study schedule
07 April 2015	- Detailed description of exploratory objectives, endpoints, and analysis - Detailed description of laboratory testing, including samples for research - Alignment of inclusion and exclusion criteria and study objectives with the updated SP003 Protocol v. 5.0 dated 15-Aug-2014. - Statistical analysis section updated - Information about phase I/II clinical trials conducted by the University Hospital in Motol updated per current knowledge - Section on concomitant medication updated - Updated safety reporting sections, including the transfer of safety monitoring responsibilities from the European Pharminvent Services to SOTIO a.s. - Introduction of new terminology: EoT, End of study, EoS visit, follow-up, and data follow-up after the EoS examinations visit - Update of the duration of the clinical trial and of the number of patients enrolled into the clinical trial - Updated section "Rationale for prostate cancer immunotherapy" - Terminology harmonization
23 July 2015	- Corrected mistake in section 6.7.5 "End of Treatment (EoT)" concerning testosterone levels per "Dear Investigator Letter" dated 19-Jun-2015 - Implementation of minor wording updates in the PV section - Clarification of the CT/bone scintigraphy schedule

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported