Clinical trial results:
Randomized, open-label, parallel-group, multi-centre phase II clinical trial with active cellular immunotherapy DCVAC/PCa in combination with hormone therapy in patients with metastatic prostate cancer

Summary

EudraCT number	2011-004986-34
Trial protocol	CZ
Global end of trial date	27 June 2016

Results information

Result version number	v1 (current)
This version publication date	05 July 2017
First version publication date	05 July 2017
Summary attachment (see zip file)	Public Disclosure Summary_SP002_Version 1.0_26-Jan-2017 (Public Disclosure Summary_SP002_Version 1.0_26-Jan-2017.pdf)

Trial information

Trial identification

Sponsor protocol code	SP002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02107391
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 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2015
Global end of trial reached?	Yes
Global end of trial date	27 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this clinical trial were to estimate the proportion of patients with PSA and disease progression within 2 years of randomization; to evaluate quality of life and pain scale scoring using the standardized European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30, version 3; and to evaluate the incidence of adverse events (AEs; with the exception of disease progression-related AEs) and overall survival.

Protection of trial subjects:

Not applicable

Background therapy:

Androgen deprivation therapy (ADT) with luteinizing hormone-releasing hormone analogs according to applicable Summaries of Product Characteristics

Evidence for comparator: -

Actual start date of recruitment	05 March 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	7 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 63
Worldwide total number of subjects	63
EEA total number of subjects	63

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)	25
From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screened: 74
Randomized: 63
Analyzed for efficacy: 63
Analyzed for safety: 61

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Control group

Arm description:

ADT alone

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Immunotherapy group

Arm description:

DCVAC/PCa in combination with ADT

Arm type	Experimental
Investigational medicinal product name	DCVAC/PCa
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 dendritic cells

Number of subjects in period 1	Control group	Immunotherapy group
Started	31	32
Completed	8	1
Not completed	23	31
Consent withdrawn by subject	4	1
Disease progression	16	25
Adverse event, non-fatal	-	1
Death due to underlying diease	2	2

Protocol deviation	1	2

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	63	63	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	25	25	
From 65-84 years	38	38	
85 years and over	0	0	
Age continuous Units: years			
median	66.5		
full range (min-max)	40.6 to 80.4	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	63	63	

Subject analysis sets

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

Subject analysis set description:

All randomized patients

Subject analysis set title	PPS
Subject analysis set type	Per protocol

Subject analysis set description:

A subset of the ITT population without patients with a significant protocol deviation and patients who did not undergo any treatment visit

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who underwent at least V1 (control group) or received at least 1 dose of DCVAC/PCa (immunotherapy group)

Reporting group values	ITT	PPS	Safety
Number of subjects	63	57	61
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)	25		
From 65-84 years	38		
85 years and over	0		
Age continuous Units: years			
median	66.5		
full range (min-max)	40.6 to 80.4		
Gender categorical Units: Subjects			
Female	0	0	0
Male	63	57	61

End points

End points reporting groups

Reporting group title	Control group
Reporting group description: ADT alone	
Reporting group title	Immunotherapy group
Reporting group description: DCVAC/PCa in combination with ADT	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized patients	
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description: A subset of the ITT population without patients with a significant protocol deviation and patients who did not undergo any treatment visit	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description: All randomized patients who underwent at least V1 (control group) or received at least 1 dose of DCVAC/PCa (immunotherapy group)	

Primary: Proportion of patients with PSA progression within 2 years after randomization

End point title	Proportion of patients with PSA progression within 2 years after randomization
End point description:	
End point type	Primary
End point timeframe: Within 2 years after randomization	

End point values	Control group	Immunotherapy group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Not applicable				
number (confidence interval 95%)	0.779 (0.599 to 0.917)	0.939 (0.765 to 0.996)		

Statistical analyses

Statistical analysis title	Primary analysis

Statistical analysis description:

The analysis of the primary endpoint, i.e., the proportion of patients with PSA progression within 2 years

after randomization, was based on time to PSA progression.

Comparison groups	Control group v Immunotherapy group
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2018
Method	Logrank

Secondary: Proportion of patients with disease progression within 2 years after randomization

End point title	Proportion of patients with disease progression within 2 years after randomization

End point description:

End point type	Secondary

End point timeframe:

Within 2 years after randomization

End point values	Control group	Immunotherapy group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Not applicable				
number (confidence interval 95%)	0.774 (0.589 to 0.904)	0.906 (0.75 to 0.98)		

Statistical analyses

Statistical analysis title	Secondary analysis
Comparison groups	Control group v Immunotherapy group
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1836
Method	Fisher exact

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe: Until the end of the study

End point values	Control group	Immunotherapy group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: months				
median (confidence interval 95%)	1000 (24.89 to 1000)	30.07 (12.85 to 1000)		

Statistical analyses

Statistical analysis title	Secondary analysis
Statistical analysis description: 1000 means "not reached"	
Comparison groups	Control group v Immunotherapy group
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0818
Method	Logrank

Secondary: Quality of life as per the standardized EORTC QLQ-C30 v3 questionnaire	
End point title	Quality of life as per the standardized EORTC QLQ-C30 v3 questionnaire
End point description: Global health status scale	
End point type	Secondary
End point timeframe: Within 2 years after randomization	

End point values	Control group	Immunotherapy group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Not applicable				
arithmetic mean (standard deviation)	60 (± 25.8)	45.8 (± 21.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain scale influence scoring as per the standardized EORTC QLQ-C30 v3 questionnaire

End point title	Pain scale influence scoring as per the standardized EORTC QLQ-C30 v3 questionnaire

End point description:

End point type	Secondary

End point timeframe:

Within 2 years after randomization

End point values	Control group	Immunotherapy group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Not applicable				
arithmetic mean (standard deviation)	22.2 (± 34.3)	28.3 (± 30.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent AEs were AEs that started or worsened during the period starting at V1 and ending 30 days after the End of treatment visit.	
Adverse event reporting additional description:	
Only treatment-emergent AEs are listed.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Control group
Reporting group description:	
ADT alone	
Reporting group title	Immunotherapy group
Reporting group description:	
DCVAC/PCa in combination with ADT	

Serious adverse events	Control group	Immunotherapy group	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)	7 / 31 (22.58%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral ischaemia			

subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 30 (3.33%)	0 / 31 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord thickening			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
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 / 31 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	0 / 30 (0.00%)	2 / 31 (6.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 31 (3.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Control group	Immunotherapy group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 30 (60.00%)	22 / 31 (70.97%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 30 (6.67%)	2 / 31 (6.45%)	
occurrences (all)	2	2	
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 31 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 30 (0.00%)	2 / 31 (6.45%)	
occurrences (all)	0	2	
Oedema peripheral			
subjects affected / exposed	2 / 30 (6.67%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 30 (0.00%)	3 / 31 (9.68%)	
occurrences (all)	0	3	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 30 (3.33%)	3 / 31 (9.68%)	
occurrences (all)	1	3	

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 30 (10.00%)	4 / 31 (12.90%)	
occurrences (all)	3	4	
Arthralgia			
subjects affected / exposed	2 / 30 (6.67%)	2 / 31 (6.45%)	
occurrences (all)	2	2	
Bone pain			
subjects affected / exposed	2 / 30 (6.67%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 30 (10.00%)	3 / 31 (9.68%)	
occurrences (all)	3	3	

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. -Definition of progression was detailed and consequently was updated secondary endpoint. -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).
07 June 2012	-Prolongation of time period for performance of leukapheresis and for leukapheresis technical feasibility assessment. -Clarification of cyclophosphamide dosing. -Clarification of active cellular immunotherapy dosing. -Inclusion criterion (Inc-3) detailed for soft-tissue metastasis. -Inclusion criterion (Inc-4) detailed for androgen deprivation therapy. -Updated SAE reporting. -Explanation added for not performing leukapheresis in control group. -Screening period prolonged. -Details provided about CT/Scintigraphy readings. -Added criteria for early patient termination in the study. -Active cellular immunotherapy transport and application description updated. -Prolonged sampling period for Immunology and Immunomonitoring to 6 months. -Explanation added that missed active cellular immunotherapy administration is not considered as a reason for termination of patient participation in the trial.
27 May 2013	-Deleted the criterion for patient early termination in the study – PSA progression with castrate levels of testosterone.
05 February 2015	-Detailed description of exploratory objectives, endpoints, and analysis. -Clearly distinguishing IMP from immune enhancers. -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: End of the Treatment, End of Study, End of Study Examination visit, Follow-up, and PSA and Survival Follow-up. -Updated timeline for clinical trial duration. -Updated section Rationale for Prostate Cancer Immunotherapy Terminology harmonization.
15 December 2015	-Information about study termination clarified -Information about study duration updated -Timing of statistical analysis described -Accord Research s.r.o. appointed for monitoring of PSA and survival follow-up data

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported