Clinical trial results:
A Phase 2, Double-Blind, Placebo Controlled Study of RV001V in Men with Biochemical Failure following Curatively Intended Therapy for Localized Prostate Cancer

Summary

EudraCT number	2019-000951-14
Trial protocol	DK FI SE DE BE GB
Global end of trial date	02 June 2022

Results information

Result version number	v1 (current)
This version publication date	06 January 2023
First version publication date	06 January 2023
Summary attachment (see zip file)	Abbreviated CSR_Synopsis (20221207 Abbreviated CSR_Synopsis (EudraCT).pdf)

Trial information

Trial identification

Sponsor protocol code	RhoVac-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03199872
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	RhoVac ApS
Sponsor organisation address	Agern Alle 24, Hørsholm, Denmark, 2970
Public contact	Malene Weis, RhoVac ApS, +45 53542818, mw@rhovac.com
Scientific contact	Malene Weis, RhoVac ApS, +45 53542818, mw@rhovac.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	18 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 May 2022
Global end of trial reached?	Yes
Global end of trial date	02 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to investigate whether a vaccination regimen with multiple subcutaneous (SC) administrations of RV001 Vaccine 0.1 mg/mL (RV001V) can reduce prostate-specific antigen (PSA) progression compared to the control group.

Protection of trial subjects:

The DMC will be advisory to the Sponsor. The DMC will periodically monitor the accumulating data from the trial, including central
laboratory data, and advise the Sponsor regarding the continuing safety of trial subjects and thoseyet to be recruited to the trial, as well as the continuing validity. The primary charge of the DMC is to monitor the study for participant safety. DMC
responsibilities include;
- Protect the safety of the study participants;
- Review and evaluate ad hoc safety issues concerning the study at the request of the sponsor;
- Make recommendations to the sponsor concerning continuation, termination, or other modifications of the study based on the observed beneficial or adverse effects of the study;
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on participant safety, scientific integrity, or the ethics of conducting the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 22
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Denmark: 72
Country: Number of subjects enrolled	Finland: 22
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	United States: 39
Worldwide total number of subjects	192
EEA total number of subjects	147

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)	43
From 65 to 84 years	146
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 257 subjects who signed the written informed consent form (IC), 192 subjects completed the screening and were enrolled in the study. For the 65 patients who were not eligible for participation, the major reason was BCR after the last definitive treatment, distant metastasis or locoregional recurrence.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Investigators, patients, and all study staff with direct patient contact were blinded to assignment to RV001V or placebo. The Interactive web response system IWRS assigned RV001V, or placebo based on a block randomization scheme.

Arms

Are arms mutually exclusive?	Yes
Arm title	RV001V group

Arm description:

RV001 vaccine 0.1 mg/mL in water-in-oil (w/o) emulsion for injection containing RV001 and the adjuvant Montanide ISA 51 were administered to subjects in the V001V arm at a dose of 0.1 mg RV001

Arm type	Experimental
Investigational medicinal product name	RV001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose of RV001 0.1 mg was given as a subcutaneous injection

Arm title	Placebo

Arm description:

Placebo vaccine containing 50/50 mixture of adjuvant and sterile acetate buffered saline pH 3.5 in a 1-mL syringe

Arm type	Placebo
Investigational medicinal product name	Placebo vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo vaccine containing 50/50 mixture of adjuvant and sterile acetate buffered saline pH 3.5 in a 1-mL syringe

Number of subjects in period 1	RV001V group	Placebo
Started	96	96
Completed	51	48
Not completed	45	48
Consent withdrawn by subject	1	1
Physician decision	2	-
Adverse event, non-fatal	1	2
Death	1	1
Primary analysis point reached prior to completion	2	6
Sponsor decision	1	-
Metastatic disease and/or PSA doubles	37	-
Metastics disease and/or PSA doubles	-	38

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	192	192	
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	70		
full range (min-max)	56 to 86	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	192	192	

Subject analysis sets

Subject analysis set title	Primary Analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Strata combined and based on the primary analysis which were conducted when 88 events had occurred in the modified intention-to-treat (m-ITT) population

Reporting group values	Primary Analysis		
Number of subjects	185		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			

Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female	0		
Male	185		

End points

End points reporting groups

Reporting group title	RV001V group

Reporting group description:

RV001 vaccine 0.1 mg/mL in water-in-oil (w/o) emulsion for injection containing RV001 and the adjuvant Montanide ISA 51 were administered to subjects in the V001V arm at a dose of 0.1 mg RV001

Reporting group title	Placebo

Reporting group description:

Placebo vaccine containing 50/50 mixture of adjuvant and sterile acetate buffered saline pH 3.5 in a 1-mL syringe

Subject analysis set title	Primary Analysis
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Strata combined and based on the primary analysis which were conducted when 88 events had occurred in the modified intention-to-treat (m-ITT) population

Primary: Primary endpoint

End point title	Primary endpoint

End point description:

The primary endpoint was defined as the time from randomization until doubling of PSA from the baseline value, clinical recurrence or death from any cause, whichever occurred first. When the subject reached a primary endpoint, he continued into the extended follow up (E-FU) phase for safety monitoring until the study was terminated 36 months after first subject's first injection. At the time of the primary analysis all subjects who have not yet reached the primary endpoint continued into E-FU for safety until study termination.

End point type	Primary

End point timeframe:

The primary endpoint was defined as the time from randomization until doubling of PSA from the baseline value

End point values	RV001V group	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	92		
Units: months				
median (confidence interval 95%)				
PSA doubling time	7.5 (5.9 to 9.2)	9.3 (7.2 to 11.3)		

Statistical analyses

Statistical analysis title	Cox regression analysis
Comparison groups	RV001V group v Placebo

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1327
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	2.07
Variability estimate	Standard deviation
Dispersion value	1.37

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Overall study period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Safety population

Reporting group description: -

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 192 (6.25%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Multiple fractures			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Lymphocele			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Incarcerated inguinal hernia			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia legionella			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal sepsis			

subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 192 (0.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	171 / 192 (89.06%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	11		
Nervous system disorders			
Dizziness			
subjects affected / exposed	18 / 192 (9.38%)		
occurrences (all)	18		
Headache			
subjects affected / exposed	41 / 192 (21.35%)		
occurrences (all)	41		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	47 / 192 (24.48%)		
occurrences (all)	47		
Injection site erythema			
subjects affected / exposed	36 / 192 (18.75%)		
occurrences (all)	36		
Injection site mass			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	11		
Injection site pain			

subjects affected / exposed	68 / 192 (35.42%)		
occurrences (all)	68		
Injection site pruritus			
subjects affected / exposed	42 / 192 (21.88%)		
occurrences (all)	42		
Injection site reaction			
subjects affected / exposed	35 / 192 (18.23%)		
occurrences (all)	35		
Injection site swelling			
subjects affected / exposed	51 / 192 (26.56%)		
occurrences (all)	51		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 192 (6.25%)		
occurrences (all)	12		
Nausea			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	11		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 192 (5.73%)		
occurrences (all)	11		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	23 / 192 (11.98%)		
occurrences (all)	23		
Myalgia			
subjects affected / exposed	23 / 192 (11.98%)		
occurrences (all)	23		
Pain in extremity			
subjects affected / exposed	19 / 192 (9.90%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2019	Revision of protocol from V1.0 to V2.0 - Front page: Short protocol name BRaVac is added to front page - Section 2.3 and 7.7.2: Exploratory endpoint C removed from protocol. - Section 6.1: Collection of archival tumor slice has been removed from the protocol. This relates to the above reasons re. the exploratory endpoint. - Section 6.1: Collection of oncology history including oncotype DX and radiation dose, in case the patient has received radiation therapy as part of previous curative treatment, has been added. This is based on recommendation from FDA received at a recent pre-IND meeting. - Section 7.3 and 9.1.1: Specification of collection of AEs/SAEs during follow up and E-follow up. AEs/SAEs are collected for 3 months post End of Treatment visit. - Section 9.11.1: Description of Dose Limiting Toxicities (DLTs) has been removed. - Section 13.1: Precision of what can be considered source document in accordance with GCP. - Section 14: Change in the publication strategy rec
15 May 2019	Protocol V2.0 to V3.0 - Synopsis: number of sites reduced from 35 to 30 - Section 4.3; Selection/Enrollment of Patients; Amended to clarify that only inclusion/exclusion data relevant to randomsiation in IWRS will be entered in IWRS - Section 5.6 Blinding and Unblinding Method; updated to clarify that the investigator can unblind a patient with our first speaking to the Medical Monitor. Where possible the Medical monitor should be consulted. - Section 9.1.1 AE Monitoring: updated to clarify that any untoward medical occurrence event that occurs after screening and before the first dose of IP will be recorded as a S(AE) - Section 9.1.2 Reporting of Adverse Events; the following text was added; - Section 9.2.1 Adverse Events; clarification that surgical procedure (pre-planned) is not considered an AE - 9.8 Reporting Serious Adverse Events, the following sentence was deleted;
13 November 2019	Protocol V3.0 to V4.0 - Specification of primary end point further with method for calculating PSA doubling - Slight revision of secondary and exploratory endpoint - Adaption of inclusion criteria - Adaption of exclusion criteria - Adding a specific benefit-risk assessment section - Safety monitorin process updated - DMC section updated
08 July 2020	Protocol V4.0 to V4.0 with Amendment #1 - Removal of Gleason score from study inclusion criteria and enrolment of patients based on PSA doubling time, to allow for inclusion of additional patients potentially benefitting from treatment - Collection of highest historical Gleason score at baseline for each patient added to assessments and procedures

26 March 2021	Protocol V4.0 with Amendment #1 to V4.0 with Amendments #1 and #2 - Correction of incorrect hemoglobin value - COVID-19 vaccination allowed during RV001 priming and maintenance treatment periods with down to 6 days following each injection - COVID-19 vaccination excluded from prohibited medications - Rewording to remove unnecessary restriction of standard diagnositcs in tumor assessments - Deletion of Annex 1: Gleason Score, as no longer applicable following amendment #1 to v4.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported