Clinical trial results:
A Randomized, Double-blind, Phase 3 Efficacy Trial of PROSTVAC-V/F ± GM-CSF in Men With Asymptomatic or Minimally Symptomatic Metastatic, Castrate-Resistant Prostate Cancer

Summary

EudraCT number	2010-021196-85
Trial protocol	GB ES BE EE IS DE DK NL PL
Global end of trial date	02 October 2017

Results information

Result version number	v1 (current)
This version publication date	04 January 2019
First version publication date	04 January 2019

Trial information

Trial identification

Sponsor protocol code	BNIT-PRV-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01322490
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bavarian Nordic, Inc.
Sponsor organisation address	3025 Carrington Mill Blvd, Suite 100, Morrisville, NC, United States, 27560
Public contact	Cesar Pico-Navarro, Bavarian Nordic, Inc., +34 628 748 006, Cesar.Pico-Navarro@bavarian-nordic.com
Scientific contact	Cesar Pico-Navarro, Bavarian Nordic, Inc., +34 628 748 006, Cesar.Pico-Navarro@bavarian-nordic.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	02 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2015
Global end of trial reached?	Yes
Global end of trial date	02 October 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To ascertain whether the survival of subjects randomized to Arm V+G (PROSTVAC-V/F plus GM-CSF) or to Arm V (PROSTVAC-V/F) is superior to that from subjects randomized to Arm P (placebo control).

Protection of trial subjects:

The investigator ensured that this clinical trial was conducted in complete accordance with the provisions of the Declaration of Helsinki (1996), the national laws and other guidelines for the conduct of clinical trials, like the ICH Harmonized Tripartite Guideline for Good Clinical Practice (GCP), to guarantee the greatest subject protection possible. Subjects had to be informed unequivocally that they were able to refuse participation in the trial, that they were able to withdraw from the trial at any time and for whatever reason, and that withdrawal of consent did not affect their subsequent medical treatment or relationship with the treating physician.

Background therapy: -

Evidence for comparator:

The trial was designed to evaluate overall survival (OS) in two separate comparisons: PROSTVAC + GM-CSF versus control, and PROSTVAC without GM-CSF versus control.

Actual start date of recruitment	28 November 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	27 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 101
Country: Number of subjects enrolled	Canada: 69
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Puerto Rico: 5
Country: Number of subjects enrolled	Russian Federation: 163
Country: Number of subjects enrolled	United States: 394
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	Spain: 126
Country: Number of subjects enrolled	United Kingdom: 99
Country: Number of subjects enrolled	Belgium: 30
Country: Number of subjects enrolled	Denmark: 108
Country: Number of subjects enrolled	Estonia: 20
Country: Number of subjects enrolled	France: 85

Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Iceland: 10
Worldwide total number of subjects	1297
EEA total number of subjects	536

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)	272
From 65 to 84 years	965
85 years and over	60

Subject disposition

Recruitment

Recruitment details:

The study population for the trial was intended to approximate the population enrolled in the randomized phase 2 trial in which an overall survival advantage was observed. Clinical trial data supported the hypothesis that patients with less aggressive and lower burden disease were more likely to benefit from therapeutic cancer vaccines.

Pre-assignment

Screening details:

Screening activities were completed within 28 days prior to the first dose of any study medication - between days -28 and -1 (Week -4 to Week 0), and were completed prior to dosing.

Period 1

Period 1 title	Treatment Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

The trial was conducted in a double-blind manner. Subjects and investigators were blinded as to their specific treatment assignment. The sponsor controlled and documented any disclosure of treatment assignments. These procedures ensured that neither the sponsor’s monitoring staff nor the investigator nor other site staff had premature access to individual subject treatment assignment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm VG (PROSTVAC + GM-CSF)

Arm description:

The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a SC GM-CSF on the day of immunization and for the subsequent three days (SC GM-CSF injection within 5 mm of the original PROSTVAC injection site).

Arm type	Experimental
Investigational medicinal product name	PROSTVAC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PROSTVAC-V for SC injection was 0.5 mL and contained at least 2 x 108 Inf.U PROSTVAC-V. PROSTVAC-F for SC injection was 0.5 mL and contained at least 1 x 109 Inf.U PROSTVAC-F.

Investigational medicinal product name	GM-CSF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GM-CSF (sargramostim; Leukine®: 250 µg, lyophilized) is a glycosylated, recombinant human GM-CSF. Lyophilized GM-CSF was reconstituted using 1.0 mL of room-temperature bacteriostatic water for injection (USP-grade or equivalent). Each 100 µg doses of GM-CSF was drawn into labeled syringes by an independent, unblinded research pharmacist or designee for use by the clinic staff or for use by individual subjects for home injection.

Arm title	Arm V (PROSTVAC + GM-CSF placebo)

Arm description:

The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a GM-CSF placebo on the day of immunization and for the subsequent three days.

Arm type	Experimental
Investigational medicinal product name	PROSTVAC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PROSTVAC-V for SC injection was 0.5 mL and contained at least 2 x 108 Inf.U PROSTVAC-V. PROSTVAC-F for SC injection was 0.5 mL and contained at least 1 x 109 Inf.U PROSTVAC-F.

Investigational medicinal product name	GM-CSF placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GM-CSF placebo was USP-grade or equivalent bacteriostatic sodium chloride (saline) for injection.

Arm title	Arm P (Vaccine placebo + GM-CSF placebo)

Arm description:

The trial treatment consisted of a single Vaccine placebo injection on Day 1 (Week 1), followed by six GM-CSF placebo injections: one injection administered at each of Weeks 3, 5, 9, 13, 17, and 21. Each Vaccine placebo injection was accompanied by administration of an GM-CSF placebo injection on the day of immunization and for three subsequent days (placebo SC injection within 5 mm of the original placebo injection site).

Arm type	Placebo
Investigational medicinal product name	Vaccine placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vaccine placebo is empty fowlpox vector matching PROSTVAC.

Investigational medicinal product name	GM-CSF placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GM-CSF placebo was USP-grade or equivalent bacteriostatic sodium chloride (saline) for injection.

Number of subjects in period 1	Arm VG (PROSTVAC + GM-CSF)	Arm V (PROSTVAC + GM-CSF placebo)	Arm P (Vaccine placebo + GM-CSF placebo)
Started	432	432	433
Completed	279	300	280
Not completed	153	132	153
Adverse event, serious fatal	7	5	3

Physician decision	2	-	1
Consent withdrawn by subject	16	14	11
Non-Compliance	-	-	1
Adverse event, non-fatal	18	12	15
Randomized but not treated	3	3	5
Other	2	2	1
Progressive Disease	100	89	112
Protocol deviation	5	7	4

Period 2

Period 2 title	Long-term Follow-up (LTFU)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm VG (PROSTVAC + GM-CSF)

Arm description:

Following the completion of the treatment phase, all subjects from Arm VG (PROSTVAC + GM-CSF) automatically entered the LTFU Phase, during which trial visits occurred every 6 months and subjects received standard-of-care treatment as determined by the investigator or treating physician. All subjects are followed for 12 months after the required number of 534 events for each between-arm comparison was reached. Concomitant medications, subject health status, disease status, newly diagnosed autoimmune diseases, and subsequent prostate cancer therapies were collected at each six-month LTFU visit.

Arm type	Experimental
Investigational medicinal product name	PROSTVAC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PROSTVAC-V for SC injection was 0.5 mL and contained at least 2 x 108 Inf.U PROSTVAC-V. PROSTVAC-F for SC injection was 0.5 mL and contained at least 1 x 109 Inf.U PROSTVAC-F.

Investigational medicinal product name	GM-CSF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GM-CSF (sargramostim; Leukine®: 250 µg, lyophilized) is a glycosylated, recombinant human GM-CSF. Lyophilized GM-CSF was reconstituted using 1.0 mL of room-temperature bacteriostatic water for injection (USP-grade or equivalent). Each 100 µg doses of GM-CSF was drawn into labeled syringes by an independent, unblinded research pharmacist or designee for use by the clinic staff or for use by individual subjects for home injection.

Arm title	Arm V (PROSTVAC + GM-CSF placebo)

Arm description:

Following the completion of the treatment phase, all subjects from Arm V (PROSTVAC + GM-CSF placebo) automatically entered the LTFU Phase, during which trial visits occurred every 6 months and subjects received standard-of-care treatment as determined by the investigator or treating physician. All subjects are followed for 12 months after the required number of 534 events for each between-arm comparison was reached. Concomitant medications, subject health status, disease status, newly diagnosed autoimmune diseases, and subsequent prostate cancer therapies were collected at each six-month LTFU visit.

Arm type	Experimental
Investigational medicinal product name	PROSTVAC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

PROSTVAC-V for SC injection was 0.5 mL and contained at least 2 x 108 Inf.U PROSTVAC-V. PROSTVAC-F for SC injection was 0.5 mL and contained at least 1 x 109 Inf.U PROSTVAC-F.

Investigational medicinal product name	GM-CSF placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GM-CSF placebo was USP-grade or equivalent bacteriostatic sodium chloride (saline) for injection.

Arm title	Arm P (Vaccine placebo + GM-CSF placebo)

Arm description:

Following the completion of the treatment phase, all subjects from Arm P (Vaccine placebo + GM-CSF placebo) automatically entered the LTFU Phase, during which trial visits occurred every 6 months and subjects received standard-of-care treatment as determined by the investigator or treating physician. All subjects are followed for 12 months after the required number of 534 events for each between-arm comparison was reached. Concomitant medications, subject health status, disease status, newly diagnosed autoimmune diseases, and subsequent prostate cancer therapies were collected at each six-month LTFU visit.

Arm type	Placebo
Investigational medicinal product name	Vaccine placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vaccine placebo is empty fowlpox vector matching PROSTVAC.

Investigational medicinal product name	GM-CSF placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GM-CSF placebo was USP-grade or equivalent bacteriostatic sodium chloride (saline) for injection.

Number of subjects in period 2	Arm VG (PROSTVAC + GM-CSF)	Arm V (PROSTVAC + GM-CSF placebo)	Arm P (Vaccine placebo + GM-CSF placebo)
Started	279	300	280
Completed	0	0	0
Not completed	408	409	413
Consent withdrawn by subject	6	9	6
Death	239	235	236
Other	2	3	2
Study Terminated by Sponsor	158	160	165
Lost to follow-up	2	2	3
Missing	1	-	1
Joined	129	109	133
Subjects Agreed to Continue into LTFU Phase	129	109	133

Baseline characteristics

Reporting groups	
Reporting group title	Arm VG (PROSTVAC + GM-CSF)
Reporting group description:	
The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a SC GM-CSF on the day of immunization and for the subsequent three days (SC GM-CSF injection within 5 mm of the original PROSTVAC injection site).	
Reporting group title	Arm V (PROSTVAC + GM-CSF placebo)
Reporting group description:	
The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a GM-CSF placebo on the day of immunization and for the subsequent three days.	
Reporting group title	Arm P (Vaccine placebo + GM-CSF placebo)
Reporting group description:	
The trial treatment consisted of a single Vaccine placebo injection on Day 1 (Week 1), followed by six GM-CSF placebo injections: one injection administered at each of Weeks 3, 5, 9, 13, 17, and 21. Each Vaccine placebo injection was accompanied by administration of an GM-CSF placebo injection on the day of immunization and for three subsequent days (placebo SC injection within 5 mm of the original placebo injection site).	

Reporting group values	Arm VG (PROSTVAC + GM-CSF)	Arm V (PROSTVAC + GM-CSF placebo)	Arm P (Vaccine placebo + GM-CSF placebo)
Number of subjects	432	432	433
Age categorical Units: Subjects			
Adults (18-64 years)	93	88	91
From 65-84 years	322	325	318
85 years and over	17	19	24
Age continuous Units: years			
arithmetic mean	70.6	71.3	71.3
full range (min-max)	45 to 90	49 to 90	46 to 93
Gender categorical Units: Subjects			
Female	0	0	0
Male	432	432	433

Reporting group values	Total		
Number of subjects	1297		
Age categorical Units: Subjects			
Adults (18-64 years)	272		
From 65-84 years	965		
85 years and over	60		
Age continuous Units: years			
arithmetic mean			
full range (min-max)	-		

Gender categorical Units: Subjects			
Female	0		
Male	1297		

Subject analysis sets

Subject analysis set title	Intent-to-Treat Set (ITT set)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intent-to-Treat Set (ITT Set) included all subjects who were randomized.	
Subject analysis set title	FAS (Full Analysis Set)
Subject analysis set type	Full analysis
Subject analysis set description: Full Analysis Set (FAS) included all subjects who initiated trial treatment.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: Safety Analysis Set included all subjects who initiated trial treatment.	

Reporting group values	Intent-to-Treat Set (ITT set)	FAS (Full Analysis Set)	Safety Analysis Set
Number of subjects	1297	1286	1286
Age categorical Units: Subjects			
Adults (18-64 years)	272	271	271
From 65-84 years	965	956	956
85 years and over	60	59	59
Age continuous Units: years			
arithmetic mean	71.1	71.1	71.1
full range (min-max)	45 to 93	45 to 93	45 to 93
Gender categorical Units: Subjects			
Female	0	0	0
Male	1297	1286	1286

End points

End points reporting groups

Reporting group title	Arm VG (PROSTVAC + GM-CSF)

Reporting group description:

The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a SC GM-CSF on the day of immunization and for the subsequent three days (SC GM-CSF injection within 5 mm of the original PROSTVAC injection site).

Reporting group title	Arm V (PROSTVAC + GM-CSF placebo)

Reporting group description:

The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a GM-CSF placebo on the day of immunization and for the subsequent three days.

Reporting group title	Arm P (Vaccine placebo + GM-CSF placebo)

Reporting group description:

The trial treatment consisted of a single Vaccine placebo injection on Day 1 (Week 1), followed by six GM-CSF placebo injections: one injection administered at each of Weeks 3, 5, 9, 13, 17, and 21. Each Vaccine placebo injection was accompanied by administration of an GM-CSF placebo injection on the day of immunization and for three subsequent days (placebo SC injection within 5 mm of the original placebo injection site).

Reporting group title	Arm VG (PROSTVAC + GM-CSF)

Reporting group description:

Following the completion of the treatment phase, all subjects from Arm VG (PROSTVAC + GM-CSF) automatically entered the LTFU Phase, during which trial visits occurred every 6 months and subjects received standard-of-care treatment as determined by the investigator or treating physician. All subjects are followed for 12 months after the required number of 534 events for each between-arm comparison was reached. Concomitant medications, subject health status, disease status, newly diagnosed autoimmune diseases, and subsequent prostate cancer therapies were collected at each six-month LTFU visit.

Reporting group title	Arm V (PROSTVAC + GM-CSF placebo)

Reporting group description:

Following the completion of the treatment phase, all subjects from Arm V (PROSTVAC + GM-CSF placebo) automatically entered the LTFU Phase, during which trial visits occurred every 6 months and subjects received standard-of-care treatment as determined by the investigator or treating physician. All subjects are followed for 12 months after the required number of 534 events for each between-arm comparison was reached. Concomitant medications, subject health status, disease status, newly diagnosed autoimmune diseases, and subsequent prostate cancer therapies were collected at each six-month LTFU visit.

Reporting group title	Arm P (Vaccine placebo + GM-CSF placebo)

Reporting group description:

Following the completion of the treatment phase, all subjects from Arm P (Vaccine placebo + GM-CSF placebo) automatically entered the LTFU Phase, during which trial visits occurred every 6 months and subjects received standard-of-care treatment as determined by the investigator or treating physician. All subjects are followed for 12 months after the required number of 534 events for each between-arm comparison was reached. Concomitant medications, subject health status, disease status, newly diagnosed autoimmune diseases, and subsequent prostate cancer therapies were collected at each six-month LTFU visit.

Subject analysis set title	Intent-to-Treat Set (ITT set)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent-to-Treat Set (ITT Set) included all subjects who were randomized.

Subject analysis set title	FAS (Full Analysis Set)
Subject analysis set type	Full analysis

Subject analysis set description:

Full Analysis Set (FAS) included all subjects who initiated trial treatment.

Subject analysis set title	Safety Analysis Set

Subject analysis set type	Safety analysis

Subject analysis set description:

Safety Analysis Set included all subjects who initiated trial treatment.

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

The primacy efficacy endpoint for the trial was OS. The survival analysis objective was to ascertain whether the survival-time distribution for subjects randomized to the investigational arm was consistent with longer survival compared to subjects randomized to the control arm. Two main overall comparisons of survival time were planned: a comparison between Arm VG and Arm P, and a comparison between Arm V and Arm P.

End point type	Primary

End point timeframe:

Overall Survival (OS) is defined as the time between the date of randomization and the date of death due to any cause.

End point values	Arm VG (PROSTVAC + GM-CSF)	Arm V (PROSTVAC + GM-CSF placebo)	Arm P (Vaccine placebo + GM-CSF placebo)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	432	432	433	
Units: Months				
median (confidence interval 95%)				
Overall Survival (months)	33.2 (30.6 to 37.4)	34.4 (31 to 36.9)	34.3 (30.7 to 37.0)	

Statistical analyses

Statistical analysis title	Statistical Analysis Plan (SAP) - Arm VG v. Arm P
Comparison groups	Arm P (Vaccine placebo + GM-CSF placebo) v Arm VG (PROSTVAC + GM-CSF)
Number of subjects included in analysis	865
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.5885
Method	Logrank

Notes:

[1] - Overall survival is calculated as the date of (death/censoring - date of randomization + 1)/30. 4375. Subjects who did not die are censored at last known alive date or datacut off date, whichever comes first. Quartiles and 95% CI are estimated using Kaplan-Meier methods. The 95% confidence intervals for the median OS times was calculated using the method by Brookmeyer and Crowley.

Statistical analysis title	Statistical Analysis Plan (SAP) - Arm V v. Arm P
Comparison groups	Arm V (PROSTVAC + GM-CSF placebo) v Arm P (Vaccine placebo + GM-CSF placebo)

Number of subjects included in analysis	865
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.4742
Method	Logrank

Notes:

[2] - Overall survival is calculated as the date of (death/censoring - date of randomization + 1)/30.4375. Subjects who did not die are censored at last known alive date or datacut off date, whichever comes first. Quartiles and 95% CI are estimated using Kaplan-Meier methods. The 95% confidence intervals for the median OS times was calculated using the method by Brookmeyer and Crowley.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The collection of AEs occurred from the signing of informed consent to 28 days following the administration of the last dose of study medication, which was approximately the Week 25/End of Treatment Visit for subjects who completed the treatment period.

Adverse event reporting additional description:

Serious Adverse Events (SAEs) if ongoing at the End of Treatment visit were followed to resolution or until the investigator assessed the subject as stable. SAEs that were reported after the end of the treatment period were collected only if they were assessed by the investigator as being possibly or definitely related to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Arm VG (PROSTVAC + GM-CSF)

Reporting group description:

The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a SC GM-CSF on the day of immunization and for the subsequent three days (SC GM-CSF injection within 5 mm of the original PROSTVAC injection site).

Reporting group title	Arm V (PROSTVAC + GM-CSF placebo)

Reporting group description:

The trial treatment consisted of a single SC injection of PROSTVAC-V on day 0 (Week 1), followed by six PROSTVAC-F injections: each administered at days 14 (Week 3), 28 (Week 5), 56 (Week 9), 84 (Week 13), 112 (Week 17), and 140 (Week 21). Each PROSTVAC injection was accompanied by a GM-CSF placebo on the day of immunization and for the subsequent three days.

Reporting group title	Arm P (Vaccine placebo + GM-CSF placebo)

Reporting group description:

The trial treatment consisted of a single Vaccine placebo injection on Day 1 (Week 1), followed by six GM-CSF placebo injections: one injection administered at each of Weeks 3, 5, 9, 13, 17, and 21. Each Vaccine placebo injection was accompanied by administration of an GM-CSF placebo injection on the day of immunization and for three subsequent days (placebo SC injection within 5 mm of the original placebo injection site).

Serious adverse events	Arm VG (PROSTVAC + GM-CSF)	Arm V (PROSTVAC + GM-CSF placebo)	Arm P (Vaccine placebo + GM-CSF placebo)
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 429 (13.05%)	56 / 429 (13.05%)	53 / 428 (12.38%)
number of deaths (all causes)	254	251	245
number of deaths resulting from adverse events	5	5	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma in situ of skin			

subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metastases to central nervous system			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Metastases to meninges			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic pain			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			

subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intermittent claudication			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular compression			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Death			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General physical health deterioration			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	2 / 429 (0.47%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	1 / 429 (0.23%)	5 / 429 (1.17%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			

subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis radiation			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun shot wound			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haematoma			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematuria			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation oesophagitis			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord injury			

subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sternal fracture			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular bypass dysfunction			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia supraventricular			

subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	3 / 428 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 429 (0.23%)	2 / 429 (0.47%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			

subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cerebrovascular accident			
subjects affected / exposed	2 / 429 (0.47%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cervical cord compression			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	2 / 429 (0.47%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nerve compression			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			

subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	4 / 429 (0.93%)	1 / 429 (0.23%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic uraemic syndrome			

subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histiocytosis haematophagic			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anal haemorrhage			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia strangulated			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 429 (0.00%)	2 / 429 (0.47%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysuria			

subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	7 / 429 (1.63%)	2 / 429 (0.47%)	4 / 428 (0.93%)
occurrences causally related to treatment / all	0 / 7	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 429 (0.23%)	5 / 429 (1.17%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive uropathy			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelocaliectasis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 429 (0.00%)	2 / 429 (0.47%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder haemorrhage			

subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	4 / 429 (0.93%)	6 / 429 (1.40%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	2 / 429 (0.47%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Appendiceal abscess			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Catheter site infection			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			

subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perinephric abscess			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 429 (0.47%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 429 (0.23%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord infection			
subjects affected / exposed	2 / 429 (0.47%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 429 (0.00%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	3 / 429 (0.70%)	1 / 429 (0.23%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	0 / 429 (0.00%)	2 / 429 (0.47%)	2 / 428 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cell death			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	1 / 428 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 429 (0.00%)	1 / 429 (0.23%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 429 (0.23%)	0 / 429 (0.00%)	0 / 428 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Arm VG (PROSTVAC + GM-CSF)	Arm V (PROSTVAC + GM-CSF placebo)	Arm P (Vaccine placebo + GM-CSF placebo)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	395 / 429 (92.07%)	386 / 429 (89.98%)	385 / 428 (89.95%)
Vascular disorders			
Hypertension			
subjects affected / exposed	23 / 429 (5.36%)	28 / 429 (6.53%)	22 / 428 (5.14%)
occurrences (all)	23	28	22
Hot flush			
subjects affected / exposed	20 / 429 (4.66%)	23 / 429 (5.36%)	12 / 428 (2.80%)
occurrences (all)	20	23	12
Nervous system disorders			
Headache			
subjects affected / exposed	43 / 429 (10.02%)	32 / 429 (7.46%)	36 / 428 (8.41%)
occurrences (all)	43	32	36
Dizziness			
subjects affected / exposed	17 / 429 (3.96%)	18 / 429 (4.20%)	22 / 428 (5.14%)
occurrences (all)	17	18	22
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	258 / 429 (60.14%)	202 / 429 (47.09%)	203 / 428 (47.43%)
occurrences (all)	258	202	203
Injection site pain			
subjects affected / exposed	131 / 429 (30.54%)	111 / 429 (25.87%)	122 / 428 (28.50%)
occurrences (all)	131	111	122
Fatigue			
subjects affected / exposed	105 / 429 (24.48%)	94 / 429 (21.91%)	91 / 428 (21.26%)
occurrences (all)	105	94	91
Injection site pruritus			
subjects affected / exposed	109 / 429 (25.41%)	77 / 429 (17.95%)	57 / 428 (13.32%)
occurrences (all)	109	77	57
Injection site swelling			
subjects affected / exposed	101 / 429 (23.54%)	73 / 429 (17.02%)	69 / 428 (16.12%)
occurrences (all)	101	73	69
Pyrexia			
subjects affected / exposed	91 / 429 (21.21%)	38 / 429 (8.86%)	53 / 428 (12.38%)
occurrences (all)	91	38	53

Injection site induration			
subjects affected / exposed	67 / 429 (15.62%)	47 / 429 (10.96%)	60 / 428 (14.02%)
occurrences (all)	67	47	60
Influenza like illness			
subjects affected / exposed	55 / 429 (12.82%)	44 / 429 (10.26%)	36 / 428 (8.41%)
occurrences (all)	55	44	36
Asthenia			
subjects affected / exposed	37 / 429 (8.62%)	32 / 429 (7.46%)	49 / 428 (11.45%)
occurrences (all)	37	32	49
Chills			
subjects affected / exposed	44 / 429 (10.26%)	34 / 429 (7.93%)	35 / 428 (8.18%)
occurrences (all)	44	34	35
Injection site oedema			
subjects affected / exposed	24 / 429 (5.59%)	22 / 429 (5.13%)	20 / 428 (4.67%)
occurrences (all)	24	22	20
Injection site warmth			
subjects affected / exposed	28 / 429 (6.53%)	15 / 429 (3.50%)	23 / 428 (5.37%)
occurrences (all)	28	15	23
Pain in extremity			
subjects affected / exposed	28 / 429 (6.53%)	28 / 429 (6.53%)	23 / 428 (5.37%)
occurrences (all)	28	28	23
Oedema peripheral			
subjects affected / exposed	24 / 429 (5.59%)	21 / 429 (4.90%)	12 / 428 (2.80%)
occurrences (all)	24	21	12
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	51 / 429 (11.89%)	51 / 429 (11.89%)	38 / 428 (8.88%)
occurrences (all)	51	51	38
Constipation			
subjects affected / exposed	26 / 429 (6.06%)	39 / 429 (9.09%)	29 / 428 (6.78%)
occurrences (all)	26	39	29
Diarrhoea			
subjects affected / exposed	29 / 429 (6.76%)	38 / 429 (8.86%)	21 / 428 (4.91%)
occurrences (all)	29	38	21
Vomiting			

subjects affected / exposed	21 / 429 (4.90%)	22 / 429 (5.13%)	17 / 428 (3.97%)
occurrences (all)	21	22	17
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	20 / 429 (4.66%)	25 / 429 (5.83%)	15 / 428 (3.50%)
occurrences (all)	20	25	15
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	18 / 429 (4.20%)	21 / 429 (4.90%)	22 / 428 (5.14%)
occurrences (all)	18	21	22
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	50 / 429 (11.66%)	49 / 429 (11.42%)	55 / 428 (12.85%)
occurrences (all)	50	49	55
Back pain			
subjects affected / exposed	43 / 429 (10.02%)	62 / 429 (14.45%)	49 / 428 (11.45%)
occurrences (all)	43	62	49
Myalgia			
subjects affected / exposed	35 / 429 (8.16%)	36 / 429 (8.39%)	43 / 428 (10.05%)
occurrences (all)	35	36	43
Musculoskeletal pain			
subjects affected / exposed	28 / 429 (6.53%)	15 / 429 (3.50%)	21 / 428 (4.91%)
occurrences (all)	28	15	21
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	18 / 429 (4.20%)	23 / 429 (5.36%)	23 / 428 (5.37%)
occurrences (all)	18	23	23
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	25 / 429 (5.83%)	39 / 429 (9.09%)	31 / 428 (7.24%)
occurrences (all)	25	39	31

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2011	Amendment 1 (dated 02 May 2011) clarified the vaccine nomenclature for consistency with all publications and trial support documents (e.g., IB, Trial Instruction Manual, etc.); changed the definition of excluded/concomitant therapies to exclude the use of secondary hormonal therapies during the Treatment Phase of the trial, and allowed the use of denosumab; restated Inclusion Criterion #5 as Exclusion Criterion #5; specified exclusion of patients receiving an investigational agent within 60 days of the first planned dose of PROSTVAC; added definition of overdose; corrected dosing information for GM-CSF; and administrative changes.
17 June 2011	Amendment 2 (dated 17 June 2011) clarified the vaccine placebo nomenclature for consistency throughout the protocol; added a placebo rationale; added language to specify who can fill syringes with investigational drug product; added Exclusion Criterion #15 and changed Exclusion Criterion #16; clarified scheduled opioid narcotic relief as a trigger for subject removal from therapy or assessment; clarified that diluent for GM-CSF and GM-CSF placebo was bacteriostatic water for injection; added explanation that laboratory procedures not routinely covered by a site's designated laboratory must be reviewed for approval by the sponsor; clarified use of a central radiological review; added language to explain use of biomarkers; clarified that peripheral blood RNA samples would be collected; and administrative changes.
12 September 2011	Amendment 3 (dated 12 September 2011) (first subject enrolled in Dec 2011) the GM-CSF reconstitution volume was changed to reflect the volumes suggested in the manufacturer's package insert; changed the GM-CSF placebo from bacteriostatic water to bacteriostatic saline; inclusion/exclusion criteria were clarified to maintain consistency with other parts of the protocol and to correct incorrectly stated units; added language to define/clarify that QOL instruments were applied where available; clarified footnote for laboratory tests to state that both troponin tests were preferred, but if only one of the troponin tests could be run, that would be accepted; added the explicit requirement for virology testing; added a specific requirement for a medical history update for newly diagnosed autoimmune diseases during LTFU; updated background material to include newly approved therapies and literature references; and administrative changes.
01 February 2012	Amendment 4 (dated 01 February 2012) revised sponsor contact information; clarified excluded chronic corticosteroid therapy; clarified Inclusion Criterion #4; revised the handling of used trial drug vials and syringes; clarified injection site management; added the QEQ-5D-3L to the QOL instruments; added the FACT-P, BPI-SF, and EQ-5D-3L to the LTFU; added calcium to the chemistry assay; clarified the sample collection time for the immune monitoring samples; revised drug accountability and reconciliation for PROSTVAC and GM-CSF to be performed by an unblinded monitor; clarified that vial numbers were recorded for drug accountability for PROSTVAC and lot numbers for GM-CSF; clarified procedures for re-screening; clarified definition of an SAE; and administrative changes.

30 May 2012	Amendment 5 (dated 30 May 2012) made changes for clarity and consistency and updated language to reflect that currently used in the field; affirmed the sponsor's commitment to compliance with ICH/ European Medicines Agency and applicable regulations; and administrative changes; updated synopsis to match protocol body; minor language revisions, updated language for consistency with IB, removed upper age limit for subjects; added language that subjects must have documented asymptomatic or minimally symptomatic mCRPC; removed language that was within the pharmacy manual and replaced with reference to the pharmacy manual; removed references to the digital; thermometer and subject diary; added section for emergency procedures; listed examples of concurrent immunotherapy and immunosuppressive therapy; moved immune monitoring assessments from screening to day 1; removed hematology and serum chemistry from LTFU; clarified that LTFU surveys would only be completed at the first LTFU visit; removed text pertaining to a local laboratory; more clearly defined AEs; added reference to pregnant partner and informed consent; made consistent with the current Management Plan for Potential Serious Vaccinia Reaction; added new section to provide greater detail regarding the key elements of ICH E2A; added new section to provide greater detail regarding documenting and reporting of AEs and SAEs in accordance with applicable global regulations; and administrative changes.
20 August 2015	Amendment 6 (dated 20 August 2015) included revision to the LTFU data collection process to increase subject retention; revision to biological and immune response assessments supporting exploratory endpoints; addition of language to clarify AE/SAE reporting requirements pertaining to progression of underlying malignancy; revised definition of analysis sets in Statistical Analysis section to align with SAP; incorporation of France- and Germany-specific protocol amendment language; and administrative changes.
07 February 2017	Amendment 7 (dated 07 February 2017) was an administrative amendment to address feedback from the Paul-Ehrlich-Institut (PEI) in Germany, who requested that the study protocol be updated to contain details regarding the Interim Analyses described in the Statistical Analysis Plan for this study. There is no impact to study design, conduct, or endpoints as a result of the language provided in protocol Section 9.8, Interim Analyses. In addition, the sponsor address and medical monitor have been updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study has discontinued due to futility.

Notes: