Clinical trial results:
A phase II trial to assess the safety, immunological activity of Trovax plus Pemetrexed/ Cisplatin in patients with malignant pleural mesothelioma.

Summary

EudraCT number	2010-023230-22
Trial protocol	GB
Global end of trial date	04 May 2016

Results information

Result version number	v1 (current)
This version publication date	04 June 2017
First version publication date	04 June 2017
Summary attachment (see zip file)	synopsis (SKOPOS synopsis.docx) consort diagram (SKOPOS consort.docx)

Trial information

Trial identification

Sponsor protocol code	2010/VCC/0049

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01569919
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Velindre NHS Trust
Sponsor organisation address	Velindre Cancer Centre, Cardiff, United Kingdom, CF14 2TL
Public contact	Joanna Canham - SKOPOS Trial Manager, Wales Cancer Trials Unit - Centre for Trials Research, 02920 687581, SKOPOS@cardiff.ac.uk
Scientific contact	Angela Casbard - SKOPOS Senior statistician , Wales Cancer Trials Unit - Centre for Trials Research, 02920 687470, SKOPOS@cardiff.ac.uk

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	15 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2016
Global end of trial reached?	Yes
Global end of trial date	04 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether TroVax® is active in the treatment of MPM. This will be assessed by measuring the cellular or humoral anti-5T4 immune responses following treatment with TroVax® given in combination with Pem/Cis.

Protection of trial subjects:

The trial involved the use of a genetically modified vaccine and this was reviewed and given ethical approval by the Gene Therapy Advisory Committee. Standard Operating procedures for the receipt, handling, storage, dispensing, transport, administration and disposal of the vaccine were put in place before the trial opened to protect patients and trial staff.

All patients were monitored for safety and serious adverse events throughout the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2013
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	United Kingdom: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

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)	10
From 65 to 84 years	19

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from Velindre Cancer Centre in Cardiff between February 2013 and December 2014.

Pre-assignment

Screening details:

Before any trial related procedures were undertaken to assess eligibility, the patient's written informed consent was obtained. Eligible patients had locally advanced or metastatic, histologically or cytologically proven MPM and were fit to take trial treatment.
37 patients were screened, 3 were not eligibile criteria and 5 patients declined.

Period 1

Period 1 title	Registration
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Experimental

Arm description:

All patients were allocated to the experimental trial treatment.

Arm type	Experimental
Investigational medicinal product name	TroVax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were given 9 intramuscular injections of TroVax®, starting two weeks before the commencement of chemotherapy, and continuing at regular intervals during and after chemotherapy. TroVax® is presented as lyophilised material. TroVax® was reconstituted by adding 1.2ml of water for injection (WFI). TroVax was given at a dose of 1 x 10^9 TCID 50/ml in 1ml by intramuscular injection into the deltoid muscle of the shoulder, given on Day 1 or 2 of weeks 1, 3, 6, 9, 12, 15, 18, 21, 24.

Number of subjects in period 1	Experimental
Started	29
Completed	29

Period 2

Period 2 title	Eligible patients
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Experimental

Arm description:

All patients were allocated to the experimental trial treatment.

Arm type	Experimental
Investigational medicinal product name	TroVax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were given 9 intramuscular injections of TroVax®, starting two weeks before the commencement of chemotherapy, and continuing at regular intervals during and after chemotherapy. TroVax® is presented as lyophilised material. TroVax® was reconstituted by adding 1.2ml of water for injection (WFI). TroVax was given at a dose of 1 x 10^9 TCID 50/ml in 1ml by intramuscular injection into the deltoid muscle of the shoulder, given on Day 1 or 2 of weeks 1, 3, 6, 9, 12, 15, 18, 21, 24.

Number of subjects in period 2	Experimental
Started	29
Completed	23
Not completed	6
Consent withdrawn by subject	3
Patient died	1
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Registration

Reporting group description: -

Reporting group values	Registration	Total	
Number of subjects	29	29	
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)	10	10	
From 65-84 years	19	19	
85 years and over	0	0	
Age continuous			
Median age of participants			
Units: years			
median	67		
inter-quartile range (Q1-Q3)	63 to 71	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	25	25	
WHO			
WHO performance status			
Units: Subjects			
WHO = 0	13	13	
WHO = 1	16	16	
Mesothelioma type Units: Subjects			
Epitheliod	20	20	
Sarcomatoid	5	5	
NOS (not otherwise specified)	4	4	
Mesothelioma stage Units: Subjects			
Stage II	11	11	
Stage III	16	16	
Stage IV	2	2	
Platelets Units: x 10^9/L			
median	313		
inter-quartile range (Q1-Q3)	250 to 405	-	

Monocytes			
Units: x 10^9/L			
median	0.7		
inter-quartile range (Q1-Q3)	0.5 to 0.8	-	
Haemoglobin			
Units: g/dl			
median	13.1		
inter-quartile range (Q1-Q3)	12.7 to 14.7	-	

Subject analysis sets

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

Subject analysis set description:

These patients received at least the first 3 TroVax injections and at least 1st cycle of chemotherapy and were confirmed to be eligible for the trial.

Reporting group values	Per protocol analysis		
Number of subjects	23		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	9		
From 65-84 years	14		
85 years and over	0		
Age continuous			
Median age of participants			
Units: years			
median	66		
inter-quartile range (Q1-Q3)	61 to 70		
Gender categorical			
Units: Subjects			
Female	3		
Male	20		
WHO			
WHO performance status			
Units: Subjects			
WHO = 0	12		
WHO = 1	11		
Mesothelioma type			
Units: Subjects			
Epitheliod	17		
Sarcomatoid	2		
NOS (not otherwise specified)	4		
Mesothelioma stage			

Units: Subjects			
Stage II	8		
Stage III	13		
Stage IV	2		
Platelets			
Units: x 10^9/L			
median	351		
inter-quartile range (Q1-Q3)	250 to 407		
Monocytes			
Units: x 10^9/L			
median	0.6		
inter-quartile range (Q1-Q3)	0.4 to 0.8		
Haemoglobin			
Units: g/dl			
median	13.8		
inter-quartile range (Q1-Q3)	12.7 to 14.7		

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description:	
All patients were allocated to the experimental trial treatment.	
Reporting group title	Experimental
Reporting group description:	
All patients were allocated to the experimental trial treatment.	
Subject analysis set title	Per protocol analysis
Subject analysis set type	Per protocol
Subject analysis set description:	
These patients received at least the first 3 TroVax injections and at least 1st cycle of chemotherapy and were confirmed to be eligible for the trial.	

Primary: Immune response to 5T4 (humoral or cellular)

End point title	Immune response to 5T4 (humoral or cellular)[1]
End point description:	
The outcome measure is the immune response to the 5T4 antigen. A success in this trial is defined as an increased response (at least a doubling in the 5T4 antibody or T-cell response) from that measured at baseline at any of the six follow-up time points. The sample size was determined using Fleming's single arm design. Using Fleming's single-stage design, p1=0.40 and p2=0.64, setting alpha=0.05 (1-sided) and 80% power, 26 participants are required. If a doubling of 5T4 immune reponse is seen in at least 16 patients, then we can reject the null hypothesis that the vaccine does not elicit an immune response.	
End point type	Primary
End point timeframe:	
The immune response is measured at six follow-up time points: after 2 injections; after 3 injections; after 4 injections; after 5 injections; after 9 injections; 10 weeks after the last injection.	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: This Fleming's design requires a threshold number of events (n=16) to be observed. We observed 22 events. No further statistical analysis was required other than counting the number of events.	

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: subjects				
Response	22			
Non-response	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

PFS is defined from the time of enrolment to any disease progression and/or death, those still progression-free and alive will be censored at the date last seen.

End point type	Secondary

End point timeframe:

Measured from time of randomisation to the time of progression or death, measured until the end of the trial.

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Months				
median (inter-quartile range (Q1-Q3))	6.8 (3.58 to 8.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

The median OS (defined as the time from enrolment to death from any cause).

End point type	Secondary

End point timeframe:

Measured from randomisation until up to two -years from randomisation.

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Months				
median (inter-quartile range (Q1-Q3))	10.87 (8.15 to 23.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival at six months

End point title	Progression free survival at six months

End point description:

End point type	Secondary

End point timeframe:

Six months from registration

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Proportion progression-free				
arithmetic mean (confidence interval 95%)	60.56 (37.83 to 77.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival at one year

End point title	Progression Free Survival at one year

End point description:

End point type	Secondary

End point timeframe:

1 year from registration

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Proportion				
arithmetic mean (confidence interval 95%)	23.29 (8.54 to 42.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival at six months

End point title	Overall survival at six months

End point description:

End point type	Secondary

End point timeframe:

six months from registration

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Proportion				
arithmetic mean (confidence interval 95%)	82.61 (60.06 to 93.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival at one year

End point title	Overall survival at one year

End point description:

End point type	Secondary

End point timeframe:

One year from registration

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Proportion				
arithmetic mean (confidence interval 95%)	43.48 (23.29 to 62.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate

End point title	Objective response rate

End point description:

The objective response rate (ORR) is defined as the number of patients with complete response or partial response.

End point type	Secondary

End point timeframe:

Up to a year from registration

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Proportion				
arithmetic mean (confidence interval 95%)	17.39 (4.95 to 38.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between baseline variables and clinical response

End point title	Relationship between baseline variables and clinical response

End point description:

The Cox proportional hazard model was used to explore whether baseline platelet levels, baseline monocyte levels and baseline haemoglobin predict time to progression. The univariable hazard ratios for each predictor are presented.

End point type	Secondary

End point timeframe:

Whole trial period

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Hazard ratio				
arithmetic mean (confidence interval 95%)				
Platelets	0.998 (0.993 to 1.003)			
Monocytes	0.6925 (0.0734 to 6.5357)			
Haemoglobin	1.2168 (0.8971 to 1.6505)			
Hematocrit*10	1.9029 (0.6279 to 5.7667)			
Mesothelin	0.9371 (0.8567 to 1.0251)			
Humoral 5T4	1.007 (0.9754 to 1.0396)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between baseline variables and immune response

End point title	Relationship between baseline variables and immune response

End point description:

A logistic regression model was used to explore the effect of haemoglobin, haematocrit soluble mesothelin and baseline 5T4 antibody level on the post treatment 5T4 antibody response.

End point type	Secondary

End point timeframe:

Whole trial period

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: Odds Ratio				
arithmetic mean (confidence interval 95%)				
Platelets	1.0564 (0.9378 to 1.19)			
Monocytes	147.61 (0.0111 to 2000000)			
Haemoglobin	0.3704 (0.0553 to 2.4822)			
Hematocrit*10	0.0324 (0.0001 to 13.6008)			
Mesothelin	1.399 (0.3872 to 5.0618)			
Humoral 5T4	1.0025 (0.8767 to 1.1462)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Humoral 5T4 overall response

End point title	Humoral 5T4 overall response

End point description:

Contributes to the primary endpoint.

End point type	Other pre-specified

End point timeframe:

The immune response is measured at six follow-up time points: after 2 injections; after 3 injections; after 4 injections; after 5 injections; after 9 injections; 10 weeks after the last injection.

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: subjects	17			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Cellular 5T4 overall response

End point title	Cellular 5T4 overall response

End point description:

Contributes to the primary endpoint.

End point type	Other pre-specified

End point timeframe:

The immune response is measured at six follow-up time points: after 2 injections; after 3 injections; after 4 injections; after 5 injections; after 9 injections; 10 weeks after the last injection.

End point values	Per protocol analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: subjects	20			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported from patient enrolment until the end of follow-up.	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.02

Reporting groups	
Reporting group title	All patients
Reporting group description:	
All patients who were registered for the trial.	

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 29 (62.07%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Phlebitis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thromboembolic event			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Cardiac arrest			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Nervous system disorders			
Altered neurology left leg paraesthesia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemia	Additional description: Ischemia cerebrovascular, Cerebral infarction		
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident	Additional description: Left Cerebrovascular accident		
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Numbness in left foot			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	2 / 29 (6.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pleural effusion	Additional description: Pleural effusion secondary to mesothelioma (previously Pulmonary Embolism)		
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleuritic pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute renal failure	Additional description: Acute kidney injury		
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations - Other, chest infection			
subjects affected / exposed	1 / 29 (3.45%)		
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	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 29 (93.10%)		
Vascular disorders			

Hypertension			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	7		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Edema limbs			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	7		
Fatigue			
subjects affected / exposed	19 / 29 (65.52%)		
occurrences (all)	33		
Fever			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	8		
Flu like symptoms			
subjects affected / exposed	7 / 29 (24.14%)		
occurrences (all)	7		
Non-Cardiac Chest pain			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	4		
Rhinorrhoea			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	6		
Immune system disorders			
Allergic reaction			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 29 (37.93%)		
occurrences (all)	22		
Dyspnea			
subjects affected / exposed	15 / 29 (51.72%)		
occurrences (all)	25		

Epistaxis subjects affected / exposed occurrences (all)	3 / 29 (10.34%) 4		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 2 / 29 (6.90%) 2 3 / 29 (10.34%) 4 2 / 29 (6.90%) 2		
Investigations Creatinine increased subjects affected / exposed occurrences (all) Neutrophil count decreased subjects affected / exposed occurrences (all) Weight loss subjects affected / exposed occurrences (all) White blood cell decreased subjects affected / exposed occurrences (all)	 2 / 29 (6.90%) 4 10 / 29 (34.48%) 14 9 / 29 (31.03%) 15 5 / 29 (17.24%) 5		
Cardiac disorders Cardiac disorders - Other, unspecified tachycardia subjects affected / exposed occurrences (all)	 5 / 29 (17.24%) 14		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dysgeusia	 7 / 29 (24.14%) 8 		

subjects affected / exposed	9 / 29 (31.03%)		
occurrences (all)	17		
Headache			
subjects affected / exposed	7 / 29 (24.14%)		
occurrences (all)	10		
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	9 / 29 (31.03%)		
occurrences (all)	14		
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Tinnitus			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	4		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Watering eyes			
subjects affected / exposed	9 / 29 (31.03%)		
occurrences (all)	17		
Gastrointestinal disorders			
Bloating			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	12 / 29 (41.38%)		
occurrences (all)	34		
Diarrhea			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	9		
Dyspepsia			

subjects affected / exposed	6 / 29 (20.69%)		
occurrences (all)	8		
Esophagitis			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	3		
Mucositis	Additional description: Location of mucositis (e.g. oral) not available		
subjects affected / exposed	14 / 29 (48.28%)		
occurrences (all)	17		
Nausea			
subjects affected / exposed	12 / 29 (41.38%)		
occurrences (all)	24		
Oral candidiasis			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	7 / 29 (24.14%)		
occurrences (all)	11		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 29 (13.79%)		
occurrences (all)	6		
Renal and urinary disorders			
Urinary frequency (nocturia)	Additional description: Nocturia		
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	3		
Urinary frequency			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	7		
Chest wall pain			
subjects affected / exposed	10 / 29 (34.48%)		
occurrences (all)	26		
Muscle weakness	Additional description: Generalized Muscle weakness		

subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorder - Other, rotator cuff pain			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	6		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	12 / 29 (41.38%)		
occurrences (all)	16		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	11 / 29 (37.93%)		
occurrences (all)	21		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2012	The was to notify the MHRA of an amendment to the Investigational Medicinal Product Dossier for Trovax for the SKOPOS trial.
28 August 2012	This substantial amendment was to support an extension for the shelf life of TroVax drug product and matching placebo, stored at ≤ -15c, from 60 months to 72 months.
23 January 2013	This substantial amendment was to notify the MHRA of an amendment to the Investigators Brochure for TroVax, to Version 9.0. The PIS was amended to Version 3.0 to include additional information on treatment side effects. In addition, the IMP labels were updated to include the vial number.
17 April 2013	This amendment was submitted to notify the MHRA of a change to the Protocol (to version 3.0) and the participant information sheet (to version 4). The protocol was updated to allow for phase I research nurses at Velindre Hospital to administer the TroVax injections in addition to the delegated clinicians. The timing of the treatment schedule was also adjusted to allow an extra day for the administration of TroVax and chemotherapy, and an extra week for a CT scan to be completed. The participant information sheet and consent form was also updated to reflect the changes to the timing of the CT scan.
03 October 2013	This substantial amendment was to support an extension for the shelf life of TroVax drug product and matching placebo.
01 April 2014	This substantial amendment was to notify the MHRA of an amendment to the Investigators Brochure for TroVax (to Version 10.0) and protocol (to Version 5.0). The protocol was updated to include changes to the blood cell count values as part of the eligibility criteria and to clarify the CT schedule and RECIST assessment. In addition, the amendment notified the MHRA of a recruitment extension until the end of October 2014.
11 November 2014	This substantial amendment was to support an extension for the shelf life of TroVax drug product and matching placebo.
23 September 2015	This substantial amendment was to notify the MHRA of an amendment to the Investigators Brochure for TroVax (to Version 11.0) and to support an extension for the shelf life of TroVax drug product and matching placebo.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported