



Clinical trial results:

An Open-Label Study of the Safety, Tolerability, and Pharmacokinetic / Pharmacodynamic Profile of VX-970 as a Single Agent in Combination With Carboplatin in Subjects With Advanced Solid Tumors

Summary

EudraCT number	2013-005100-34
Trial protocol	GB
Global end of trial date	10 January 2018

Results information

Result version number	v1 (current)
This version publication date	26 January 2019
First version publication date	26 January 2019

Trial information

Trial identification

Sponsor protocol code	VX13-970-002
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, United States,
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 8776348789, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 8776348789, medicalinfo@vrtx.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 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2018
Global end of trial reached?	Yes
Global end of trial date	10 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of VX-970 in subjects with advanced solid tumors.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Council on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	43
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This is an open-label study conducted in 5 parts (Parts A1, A2, B1, B2 and C).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A (A1 and A2)

Arm description:

Subjects received VX-970 once-weekly (Part A1) and twice-weekly (Part A2) as a single agent.

Arm type	Experimental
Investigational medicinal product name	VX-970
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose of VX-970 was infused intravenously over 60 minutes ($\pm$ 10 minutes).

Arm title	Part B1
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Arm description:

Subjects received VX-970 in combination with carboplatin.

Arm type	Experimental
Investigational medicinal product name	VX-970
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose of VX-970 was infused intravenously over 60 minutes ($\pm$ 10 minutes).

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was administered as per institutional standards (up to area under the concentration versus time curve [AUC] = 6 milligram/milliliter*minute [mg/mL*min]).

Arm title	Part B2
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Arm description:

Subjects received VX-970 in combination with carboplatin and paclitaxel.

Arm type	Experimental
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Investigational medicinal product name	VX-970
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose of VX-970 was infused intravenously over 60 minutes ($\pm$ 10 minutes).

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was administered as per institutional standards (up to area under the concentration versus time curve [AUC] = 6 milligram/milliliter*minute [mg/mL*min]).

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel was administered as per institutional standards (up to 225 mg/square meter).

Arm title	Part C
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Arm description:

Subjects received VX-970 as a single agent, followed by administration of VX-970 in combination with carboplatin.

Arm type	Experimental
Investigational medicinal product name	VX-970
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose of VX-970 was infused intravenously over 60 minutes ($\pm$ 10 minutes).

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was administered as per institutional standards (up to AUC = 6 mg/mL*min).

Number of subjects in period 1	Part A (A1 and A2)	Part B1	Part B2
Started	17	23	15
Completed	16	21	14
Not completed	1	2	1
Physician Decision	-	-	1
Death	1	-	-

Other	-	2	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Part C
Started	15
Completed	13
Not completed	2
Physician Decision	-
Death	1
Other	-
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Part A (A1 and A2)
Reporting group description:	
Subjects received VX-970 once-weekly (Part A1) and twice-weekly (Part A2) as a single agent.	
Reporting group title	Part B1
Reporting group description:	
Subjects received VX-970 in combination with carboplatin.	
Reporting group title	Part B2
Reporting group description:	
Subjects received VX-970 in combination with carboplatin and paclitaxel.	
Reporting group title	Part C
Reporting group description:	
Subjects received VX-970 as a single agent, followed by administration of VX-970 in combination with carboplatin.	

Reporting group values	Part A (A1 and A2)	Part B1	Part B2
Number of subjects	17	23	15
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	63.4	62.0	54.6
standard deviation	± 10.3	± 8.8	± 9.2
Gender categorical			
Units: Subjects			
Female	10	15	10
Male	7	8	5

Reporting group values	Part C	Total	
Number of subjects	15	70	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	60.5		
standard deviation	± 10.3	-	
Gender categorical			
Units: Subjects			
Female	8	43	
Male	7	27	

End points

End points reporting groups

Reporting group title	Part A (A1 and A2)
Reporting group description: Subjects received VX-970 once-weekly (Part A1) and twice-weekly (Part A2) as a single agent.	
Reporting group title	Part B1
Reporting group description: Subjects received VX-970 in combination with carboplatin.	
Reporting group title	Part B2
Reporting group description: Subjects received VX-970 in combination with carboplatin and paclitaxel.	
Reporting group title	Part C
Reporting group description: Subjects received VX-970 as a single agent, followed by administration of VX-970 in combination with carboplatin.	

Primary: Number of Subjects With Treatment-emergent Adverse Event (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Event (AEs) and Serious Adverse Events (SAEs) ^[1]
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End point description:

End point type	Primary
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End point timeframe:

From first dose of Study Drug through Safety Follow-up Visit

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: Only descriptive statistics were planned. No statistical comparisons were planned for primary safety endpoint.

End point values	Part A (A1 and A2)	Part B1	Part B2	Part C
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	23	15	15
Units: Subjects				
Subjects with TEAEs	17	23	15	15
Subjects With Serious TEAEs	8	8	7	9

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of Study Drug through Safety Follow-up Visit

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18
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Reporting groups

Reporting group title	Part A (A1 and A2)
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Reporting group description: -

Reporting group title	Part B1
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Reporting group description: -

Reporting group title	Part B2
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Reporting group description: -

Reporting group title	Part C
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Reporting group description: -

Serious adverse events	Part A (A1 and A2)	Part B1	Part B2
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 17 (47.06%)	8 / 23 (34.78%)	7 / 15 (46.67%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 17 (11.76%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Malignant ascites			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (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
Metastases to liver			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (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 / 17 (0.00%)	1 / 23 (4.35%)	0 / 15 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (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
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	3 / 23 (13.04%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)	1 / 23 (4.35%)	0 / 15 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 17 (5.88%)	1 / 23 (4.35%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			

subjects affected / exposed	0 / 17 (0.00%)	1 / 23 (4.35%)	0 / 15 (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
Atelectasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 17 (0.00%)	2 / 23 (8.70%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	1 / 17 (5.88%)	1 / 23 (4.35%)	0 / 15 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 23 (4.35%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 17 (0.00%)	1 / 23 (4.35%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 23 (4.35%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	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 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	1 / 23 (4.35%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part C		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 15 (60.00%)		
number of deaths (all causes)	1		

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant ascites			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to liver			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to central nervous system			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleuritic pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nausea			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Oesophageal obstruction			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)		
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	Part A (A1 and A2)	Part B1	Part B2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	23 / 23 (100.00%)	15 / 15 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	3 / 17 (17.65%)	0 / 23 (0.00%)	2 / 15 (13.33%)
occurrences (all)	4	0	3
Vascular disorders			
Flushing			
subjects affected / exposed	4 / 17 (23.53%)	4 / 23 (17.39%)	0 / 15 (0.00%)
occurrences (all)	12	4	0
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Phlebitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Hot flush			

subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Superior vena cava occlusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 17 (35.29%)	11 / 23 (47.83%)	8 / 15 (53.33%)
occurrences (all)	8	17	8
Catheter site erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Catheter site inflammation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Catheter site phlebitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Catheter site related reaction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	1 / 17 (5.88%)	2 / 23 (8.70%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Injection site rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Local swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			

subjects affected / exposed	1 / 17 (5.88%)	2 / 23 (8.70%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Peripheral swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Infusion site erythema			
subjects affected / exposed	0 / 17 (0.00%)	2 / 23 (8.70%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Infusion site extravasation			
subjects affected / exposed	0 / 17 (0.00%)	2 / 23 (8.70%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Infusion site paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infusion site reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Pelvic discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 17 (11.76%)	4 / 23 (17.39%)	1 / 15 (6.67%)
occurrences (all)	2	6	1
Oropharyngeal pain			

subjects affected / exposed	2 / 17 (11.76%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
Dyspnoea			
subjects affected / exposed	1 / 17 (5.88%)	4 / 23 (17.39%)	1 / 15 (6.67%)
occurrences (all)	1	4	1
Productive cough			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 17 (17.65%)	0 / 23 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	3 / 15 (20.00%)
occurrences (all)	1	0	3
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			

subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 17 (11.76%)	2 / 23 (8.70%)	5 / 15 (33.33%)
occurrences (all)	3	2	7
Fall			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Incisional hernia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Post procedural discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Stoma site erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Cardiac disorders			

Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 23 (0.00%) 0	1 / 15 (6.67%) 1
Palpitations subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	2 / 23 (8.70%) 3	0 / 15 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	2 / 23 (8.70%) 2	2 / 15 (13.33%) 2
Sciatica subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	4 / 23 (17.39%) 4	1 / 15 (6.67%) 1
Dizziness subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 23 (0.00%) 0	2 / 15 (13.33%) 2
Hyperaesthesia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 23 (0.00%) 0	1 / 15 (6.67%) 1
Spinal cord compression subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 23 (0.00%) 0	0 / 15 (0.00%) 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	5 / 17 (29.41%)	13 / 23 (56.52%)	7 / 15 (46.67%)
occurrences (all)	5	21	9
Leukocytosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 17 (0.00%)	11 / 23 (47.83%)	9 / 15 (60.00%)
occurrences (all)	0	31	18
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	9 / 23 (39.13%)	5 / 15 (33.33%)
occurrences (all)	0	23	7
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 17 (35.29%)	12 / 23 (52.17%)	7 / 15 (46.67%)
occurrences (all)	8	17	7
Diarrhoea			
subjects affected / exposed	4 / 17 (23.53%)	4 / 23 (17.39%)	2 / 15 (13.33%)
occurrences (all)	5	6	3
Vomiting			
subjects affected / exposed	4 / 17 (23.53%)	2 / 23 (8.70%)	4 / 15 (26.67%)
occurrences (all)	6	3	5
Constipation			
subjects affected / exposed	2 / 17 (11.76%)	8 / 23 (34.78%)	2 / 15 (13.33%)
occurrences (all)	2	8	2
Abdominal discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			

subjects affected / exposed	1 / 17 (5.88%)	4 / 23 (17.39%)	1 / 15 (6.67%)
occurrences (all)	1	6	1
Abdominal pain upper			
subjects affected / exposed	1 / 17 (5.88%)	2 / 23 (8.70%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Small intestinal haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Dyspepsia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	0	3
Oral pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)	4 / 23 (17.39%)	0 / 15 (0.00%)
occurrences (all)	2	4	0
Decubitus ulcer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pruritus allergic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 17 (5.88%)	3 / 23 (13.04%)	0 / 15 (0.00%)
occurrences (all)	3	3	0
Rash macular			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1

Urticaria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 23 (8.70%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Erythema			
subjects affected / exposed	0 / 17 (0.00%)	2 / 23 (8.70%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Rash maculo-papular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pollakiuria			

subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 23 (8.70%)	5 / 15 (33.33%)
occurrences (all)	2	3	5
Groin pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 23 (8.70%)	4 / 15 (26.67%)
occurrences (all)	1	2	5
Pain in extremity			
subjects affected / exposed	1 / 17 (5.88%)	2 / 23 (8.70%)	0 / 15 (0.00%)
occurrences (all)	1	2	0
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	6 / 23 (26.09%)	1 / 15 (6.67%)
occurrences (all)	0	7	1
Muscular weakness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 17 (23.53%)	5 / 23 (21.74%)	0 / 15 (0.00%)
occurrences (all)	7	6	0
Bronchitis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Parotitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	2 / 23 (8.70%)	1 / 15 (6.67%)
occurrences (all)	1	3	1
Respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Urinary tract infection bacterial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	3 / 17 (17.65%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	3	0	0
Decreased appetite			
subjects affected / exposed	2 / 17 (11.76%)	3 / 23 (13.04%)	1 / 15 (6.67%)
occurrences (all)	2	4	1
Hypokalaemia			
subjects affected / exposed	2 / 17 (11.76%)	5 / 23 (21.74%)	2 / 15 (13.33%)
occurrences (all)	9	8	2

Hyponatraemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Hypophosphataemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 23 (0.00%)	0 / 15 (0.00%)
occurrences (all)	2	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 17 (0.00%)	3 / 23 (13.04%)	2 / 15 (13.33%)
occurrences (all)	0	4	2

Non-serious adverse events	Part C		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Phlebitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Superior vena cava occlusion			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Venous thrombosis			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	7		
Catheter site erythema			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Catheter site inflammation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Catheter site phlebitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Catheter site related reaction			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injection site rash			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Local swelling			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Infusion site erythema			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Infusion site extravasation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Infusion site paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Infusion site reaction			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Face oedema			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Pelvic discomfort			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Productive cough			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood pressure increased			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	5 / 15 (33.33%)		
occurrences (all)	6		
Fall			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Incisional hernia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Post procedural discomfort			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Stoma site erythema			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Foot fracture			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	4		
Dysgeusia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Hyperaesthesia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Spinal cord compression			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	7		
Leukocytosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Neutropenia			

subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	4		
Thrombocytopenia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 15 (73.33%)		
occurrences (all)	12		
Diarrhoea			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Small intestinal haemorrhage			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Decubitus ulcer			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Night sweats			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pruritus allergic			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rash macular			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Erythema			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pruritus generalised			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Swelling face			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Micturition urgency			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	4		
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Parotitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Urinary tract infection bacterial			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Hypokalaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2014	Changed genomic DNA sample source from blood to saliva and decreased the number of plasma DNA collection time points; Updated appropriate texts to improve clarity and consistency; Updates to support PK assessments; Clarified stopping rule for subjects with progressive disease; Removed exclusion criterion for subjects receiving medications that are mainly metabolized by CYP3A4
22 January 2015	Dose escalation for subjects in Part B was modified to allow escalation of carboplatin; Clarified the timed tumor biopsy pharmacokinetic sample collection for Part B subjects
28 May 2015	Subpart A2 was added to evaluate the safety and tolerability of twice-weekly dosing of single-agent VX-970; Part B was revised to include subpart B2 to evaluate the safety and tolerability of VX-970 in combination with carboplatin and paclitaxel; Part C study population was clarified; Dose Limiting Toxicity (DLT) definition was modified; Inclusion/Exclusion criteria were modified; Follow-up assessments were modified
12 May 2016	Dose escalation schema for Part B2 was modified; Exclusion criterion added to exclude subjects who have been diagnosed with Li-Fraumeni Syndrome or ataxia telangiectasia

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported