Clinical trial results:
A Phase 1/2, Multicenter, Open-Label, Dose-Finding Study To Assess The Safety, Tolerability, And Preliminary Efficacy Of Weekly Nab®-Paclitaxel In Pediatric Patients With Recurrent Or Refractory Solid Tumors

Summary

EudraCT number	2013-000144-26
Trial protocol	IT GB FR ES Outside EU/EEA
Global end of trial date	06 November 2018

Results information

Result version number	v1 (current)
This version publication date	19 May 2019
First version publication date	19 May 2019

Trial information

Trial identification

Sponsor protocol code	ABI-007-PST-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01962103
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	86 Morris Avenue, Summit, United States, 07901
Public contact	Clinical Trial Disclosure, Celgene Corporation, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com
Scientific contact	Ileana Elias, MD, Celgene Corporation, 01 647-968-4300, ILElias@celgene.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001308-PIP01-12
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	06 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase 1 portion: To determine the pediatric maximum tolerated dose (MTD)/ pediatric recommended Phase 2 dose (RP2D), safety and tolerability Phase 2 portion: To characterize antitumor activity at RP2D assessed by overall response rate (ORR)

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection, Archiving of Essential Documents

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	107
EEA total number of subjects	93

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	1

months)	
Children (2-11 years)	54
Adolescents (12-17 years)	49
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

20 sites from the following countries enrolled subjects from: Canada, France, Italy, Spain, Switzerland, United Kingdom, and the United States.

Pre-assignment

Screening details:

Sixty-five subjects were included in the Phase 1 enrolled population, and 64 enrolled subjects received at least 1 dose of study drug and were included in the safety population, noted below. Forty-two subjects were included in the Phase 2 enrolled and safety populations.

Period 1

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

Blinding implementation details:

Phase 1 was a rolling-6, dose-finding structure.

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: Nab-Paclitaxel 120 mg/m^2

Arm description:

nab-paclitaxel 120 mg/m^2 intravenously (IV) on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the recommended phase 2 dose (RP2D).

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

nab-paclitaxel 120 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 1: Nab-Paclitaxel 150 mg/m^2

Arm description:

nab-paclitaxel 150 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

nab-paclitaxel 150 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 1: Nab-Paclitaxel 180 mg/m^2

Arm description:

nab-paclitaxel 180 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Arm type	Experimental

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

Dosage and administration details:

nab-paclitaxel 180 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 1: Nab-Paclitaxel 210 mg/m^2

Arm description:

nab-paclitaxel 210 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

nab-paclitaxel 210 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 1: Nab-Paclitaxel 240 mg/m^2

Arm description:

nab-paclitaxel 240 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

nab-paclitaxel 240 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 1: Nab-Paclitaxel 270 mg/m^2

Arm description:

nab-paclitaxel 270 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

nab-paclitaxel 270 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 2: Ewing's Sarcoma

Arm description:

Subjects with Ewing's sarcoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.

Arm type	Experimental

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

Dosage and administration details:

nab-paclitaxel 240 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 2: Neuroblastoma

Arm description:

Subjects with neuroblastoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

nab-paclitaxel 240 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Arm title	Phase 2: Rhabdomyosarcoma

Arm description:

Subjects with rhabdomyosarcoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	nab-Paclitaxel
Investigational medicinal product code	
Other name	Abraxane
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

nab-paclitaxel 240 mg/m^2 by IV infusion on Days 1, 8 and 15 of each 28-day cycle

Number of subjects in period 1[1]	Phase 1: Nab-Paclitaxel 120 mg/m^2	Phase 1: Nab-Paclitaxel 150 mg/m^2	Phase 1: Nab-Paclitaxel 180 mg/m^2
Started	16	8	14
Completed	2	1	3
Not completed	14	7	11
Death	14	7	11
Withdrawal by Parent/Guardian	-	-	-
Lost to follow-up	-	-	

Completed	6	0	1
Not completed	5	8	6
Death	5	8	4
Withdrawal by Parent/Guardian	-	-	-
Lost to follow-up	-	-	1
Other, Not Specified	-	-	1

Number of subjects in period 1[1]	Phase 2: Ewing's Sarcoma	Phase 2: Neuroblastoma	Phase 2: Rhabdomyosarcoma
Started	14	14	14
Completed	2	4	1
Not completed	12	10	13
Death	11	10	12
Withdrawal by Parent/Guardian	-	-	1
Lost to follow-up	1	-	-
Other, Not Specified	-	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 107 subjects were included in the enrolled population, and only 106 enrolled subjects received at least 1 dose of study drug.

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1: Nab-Paclitaxel 120 mg/m^2
Reporting group description:	
nab-paclitaxel 120 mg/m^2 intravenously (IV) on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the recommended phase 2 dose (RP2D).	
Reporting group title	Phase 1: Nab-Paclitaxel 150 mg/m^2
Reporting group description:	
nab-paclitaxel 150 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 180 mg/m^2
Reporting group description:	
nab-paclitaxel 180 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 210 mg/m^2
Reporting group description:	
nab-paclitaxel 210 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 240 mg/m^2
Reporting group description:	
nab-paclitaxel 240 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 270 mg/m^2
Reporting group description:	
nab-paclitaxel 270 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 2: Ewing's Sarcoma
Reporting group description:	
Subjects with Ewing's sarcoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.	
Reporting group title	Phase 2: Neuroblastoma
Reporting group description:	
Subjects with neuroblastoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.	
Reporting group title	Phase 2: Rhabdomyosarcoma
Reporting group description:	
Subjects with rhabdomyosarcoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.	

Reporting group values	Phase 1: Nab-Paclitaxel 120 mg/m^2	Phase 1: Nab-Paclitaxel 150 mg/m^2	Phase 1: Nab-Paclitaxel 180 mg/m^2
Number of subjects	16	8	14
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	11.7	12.1	10.2
standard deviation	± 3.32	± 5.84	± 4.64
Sex: Female, Male Units: Subjects			
Female	9	4	9
Male	7	4	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	3	1
Not Hispanic or Latino	6	5	7
Unknown or Not Reported	8	0	6
Race/Ethnicity, Customized Units: Subjects			
White	11	8	9
Not Collected or Reported	5	0	5
Other, Not Specified	0	0	0
Black or African American	0	0	0
Subjects With Any Prior Cancer Treatment Units: Subjects			
Any Prior Cancer Treatment	16	8	14
Number of Prior Systemic Anticancer Regimens Received Units: systemic anticancer regimens			
arithmetic mean	3.69	3.25	3.64
standard deviation	± 1.815	± 1.832	± 1.946

Reporting group values	Phase 1: Nab-Paclitaxel 210 mg/m^2	Phase 1: Nab-Paclitaxel 240 mg/m^2	Phase 1: Nab-Paclitaxel 270 mg/m^2
Number of subjects	11	8	7
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	10.2	11.6	12.1
standard deviation	± 5.36	± 4.63	± 2.97
Sex: Female, Male Units: Subjects			
Female	7	1	3
Male	4	7	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	3	0
Not Hispanic or Latino	10	5	5
Unknown or Not Reported	0	0	2
Race/Ethnicity, Customized Units: Subjects			
White	9	8	5
Not Collected or Reported	0	0	1

Other, Not Specified	2	0	1
Black or African American	0	0	0
Subjects With Any Prior Cancer Treatment Units: Subjects			
Any Prior Cancer Treatment	11	8	7
Number of Prior Systemic Anticancer Regimens Received Units: systemic anticancer regimens			
arithmetic mean	3.64	3.00	3.00
standard deviation	± 2.461	± 1.309	± 0.816

Reporting group values	Phase 2: Ewing's Sarcoma	Phase 2: Neuroblastoma	Phase 2: Rhabdomyosarcoma
Number of subjects	14	14	14
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	10.1	7.1	12.4
standard deviation	± 4.63	± 3.42	± 6.42
Sex: Female, Male Units: Subjects			
Female	6	5	9
Male	8	9	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	2	5
Not Hispanic or Latino	11	8	8
Unknown or Not Reported	3	4	1
Race/Ethnicity, Customized Units: Subjects			
White	11	11	12
Not Collected or Reported	3	3	1
Other, Not Specified	0	0	0
Black or African American	0	0	1
Subjects With Any Prior Cancer Treatment Units: Subjects			
Any Prior Cancer Treatment	14	14	14
Number of Prior Systemic Anticancer Regimens Received Units: systemic anticancer regimens			
arithmetic mean	2.50	2.14	2.21
standard deviation	± 0.519	± 0.663	± 0.579

Reporting group values	Total		
Number of subjects	106		
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Subjects			
Female	53		
Male	53		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	17		
Not Hispanic or Latino	65		
Unknown or Not Reported	24		
Race/Ethnicity, Customized Units: Subjects			
White	84		
Not Collected or Reported	18		
Other, Not Specified	3		
Black or African American	1		
Subjects With Any Prior Cancer Treatment Units: Subjects			
Any Prior Cancer Treatment	106		
Number of Prior Systemic Anticancer Regimens Received Units: systemic anticancer regimens arithmetic mean standard deviation	- -		

End points

End points reporting groups

Reporting group title	Phase 1: Nab-Paclitaxel 120 mg/m^2
Reporting group description:	
nab-paclitaxel 120 mg/m^2 intravenously (IV) on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the recommended phase 2 dose (RP2D).	
Reporting group title	Phase 1: Nab-Paclitaxel 150 mg/m^2
Reporting group description:	
nab-paclitaxel 150 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 180 mg/m^2
Reporting group description:	
nab-paclitaxel 180 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 210 mg/m^2
Reporting group description:	
nab-paclitaxel 210 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 240 mg/m^2
Reporting group description:	
nab-paclitaxel 240 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 1: Nab-Paclitaxel 270 mg/m^2
Reporting group description:	
nab-paclitaxel 270 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.	
Reporting group title	Phase 2: Ewing's Sarcoma
Reporting group description:	
Subjects with Ewing's sarcoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.	
Reporting group title	Phase 2: Neuroblastoma
Reporting group description:	
Subjects with neuroblastoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.	
Reporting group title	Phase 2: Rhabdomyosarcoma
Reporting group description:	
Subjects with rhabdomyosarcoma: nab-paclitaxel at the RP2D (240 mg/m^2 in subjects weighing > 10 kg and 11.5 mg/kg in subjects weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.	
Subject analysis set title	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the Phase 1: Nab-Paclitaxel 120 mg/m^2 reporting group who received at least one dose of nab-paclitaxel and had evaluable concentration data.	
Subject analysis set title	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the Phase 1: Nab-Paclitaxel 150 mg/m^2 reporting group who received at least one dose of nab-paclitaxel and had evaluable concentration data.	
Subject analysis set title	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180

	mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the Phase 1: Nab-Paclitaxel 180 mg/m^2 reporting group who received at least one dose of nab-paclitaxel and had evaluable concentration data.

Subject analysis set title	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the Phase 1: Nab-Paclitaxel 210 mg/m^2 reporting group who received at least one dose of nab-paclitaxel and had evaluable concentration data.

Subject analysis set title	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the Phase 1: Nab-Paclitaxel 240 mg/m^2 reporting group who received at least one dose of nab-paclitaxel and had evaluable concentration data.

Subject analysis set title	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the Phase 1: Nab-Paclitaxel 270 mg/m^2 reporting group who received at least one dose of nab-paclitaxel and had evaluable concentration data.

Subject analysis set title	Pharmacokinetic Population
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who received at least one dose of nab-paclitaxel and had evaluable concentration data.

Subject analysis set title	Dose Determining Set: Phase 1: Nab-Paclitaxel 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All Phase 1 subjects in the Phase 1: Nab-Paclitaxel 120 mg/m^2 reporting group who received all 3 weekly doses of nab-paclitaxel at the cohort planned dose during Cycle 1 and had adequate safety assessments during the DLT assessment period or experienced a DLT. The DDS did not include subjects who were enrolled at each dose once the dose had been determined to be safe.

Subject analysis set title	Dose Determining Set: Phase 1: Nab-Paclitaxel 150 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All Phase 1 subjects in the Phase 1: Nab-Paclitaxel 150 mg/m^2 reporting group who received all 3 weekly doses of nab-paclitaxel at the cohort planned dose during Cycle 1 and had adequate safety assessments during the DLT assessment period or experienced a DLT. The DDS did not include subjects who were enrolled at each dose once the dose had been determined to be safe.

Subject analysis set title	Dose Determining Set: Phase 1: Nab-Paclitaxel 180 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All Phase 1 subjects in the Phase 1: Nab-Paclitaxel 180 mg/m^2 reporting group who received all 3 weekly doses of nab-paclitaxel at the cohort planned dose during Cycle 1 and had adequate safety assessments during the DLT assessment period or experienced a DLT. The DDS did not include subjects who were enrolled at each dose once the dose had been determined to be safe.

Subject analysis set title	Dose Determining Set: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All Phase 1 subjects in the Phase 1: Nab-Paclitaxel 210 mg/m^2 reporting group who received all 3 weekly doses of nab-paclitaxel at the cohort planned dose during Cycle 1 and had adequate safety assessments during the DLT assessment period or experienced a DLT. The DDS did not include subjects who were enrolled at each dose once the dose had been determined to be safe.

Subject analysis set title	Dose Determining Set: Phase 1: Nab-Paclitaxel 240 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All Phase 1 subjects in the Phase 1: Nab-Paclitaxel 240 mg/m^2 reporting group who received all 3 weekly doses of nab-paclitaxel at the cohort planned dose during Cycle 1 and had adequate safety assessments during the DLT assessment period or experienced a DLT. The DDS did not include subjects who were enrolled at each dose once the dose had been determined to be safe.

Subject analysis set title	Dose Determining Set: Phase 1: Nab-Paclitaxel 270 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

All Phase 1 subjects in the Phase 1: Nab-Paclitaxel 270 mg/m^2 reporting group who received all 3 weekly doses of nab-paclitaxel at the cohort planned dose during Cycle 1 and had adequate safety assessments during the DLT assessment period or experienced a DLT. The DDS did not include subjects who were enrolled at each dose once the dose had been determined to be safe.

Subject analysis set title	Efficacy Evaluable Population: Phase 2: Ewing's Sarcoma
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 2: Ewing's Sarcoma reporting group who met eligibility criteria for Phase 2, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 2: Neuroblastoma
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 2: Neuroblastoma reporting group who met eligibility criteria for Phase 2, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 2: Rhabdomyosarcoma
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 2: Rhabdomyosarcoma reporting group who met eligibility criteria for Phase 2, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 120 mg/
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 1: Nab-Paclitaxel 120 mg/m^2 reporting group who met eligibility criteria for Phase 1, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 150 mg/
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 1: Nab-Paclitaxel 150 mg/m^2 reporting group who met eligibility criteria for Phase 1, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 180 mg/
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 1: Nab-Paclitaxel 180 mg/m^2 reporting group who met eligibility criteria for Phase 1, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 210 mg/
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 1: Nab-Paclitaxel 210 mg/m^2 reporting group who met eligibility criteria for Phase 1, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy

assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 240 mg/
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 1: Nab-Paclitaxel 240 mg/m^2 reporting group who met eligibility criteria for Phase 1, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Subject analysis set title	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 270 mg/
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects in the Phase 1: Nab-Paclitaxel 270 mg/m^2 reporting group who met eligibility criteria for Phase 1, completed at least 1 dose of study drug, and had baseline and at least 1 postbaseline efficacy assessment if having not discontinued the investigational product prior to postbaseline efficacy assessment due to disease progression or systematic deterioration.

Primary: Phase 1: Number of Subjects With Dose Limiting Toxicities (DLTs)

End point title	Phase 1: Number of Subjects With Dose Limiting Toxicities (DLTs)[1]

End point description:

A DLT = investigational product (IP) related adverse event occurring during the DLT assessment period that led to treatment discontinuation or met one of the following criteria: Common Terminology Criteria for Adverse Events (CTCAE) Grade (Gr) 3 or 4 nonhematologic toxicity (excluding transient transaminitis); CTCAE Gr 3 or 4 nausea or vomiting that persisted > 5 days despite maximal anti-emetic treatment; CTCAE Gr 4 thrombocytopenia or anemia that persisted > 7 days or required transfusion > 7 days; CTCAE Gr 3 thrombocytopenia with bleeding; CTCAE Gr 4 uncomplicated neutropenia lasting > 7 days; Febrile neutropenia with confirmed bacterial infection; CTCAE Gr 3 hematologic toxicity requiring treatment delay > 21 days. Use of "..." in the table rows signifies the continuation of row title per the above list.

End point type	Primary

End point timeframe:

DLT assessment period: For subjects > 10 kg: the first 28-day cycle including Cycle 2 Day 1 predose evaluations; for subjects ≤ 10 kg: the first two 28-day cycles including Cycle 3 Day 1 predose evaluations

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: Endpoint data presented for Phase 1 only, per protocol.

End point values	Dose Determining Set: Phase 1: Nab-Paclitaxel 120 mg/m^2	Dose Determining Set: Phase 1: Nab-Paclitaxel 150 mg/m^2	Dose Determining Set: Phase 1: Nab-Paclitaxel 180 mg/m^2	Dose Determining Set: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: subjects				
At least 1 DLT	1	0	0	0
Gr 3/4 Nonhematologic Toxicity...	1	0	0	0
Gr 3/4 Nausea or Vomiting Persisting >5 days...	0	0	0	0
Gr 4 Thrombocytopenia/Anemia Persisting >7 days...	0	0	0	0
Gr 3 Thrombocytopenia with Bleeding	0	0	0	0
Gr 4 Uncomplicated Neutropenia Lasting >7 days	0	0	0	0
Febrile Neutropenia+Confirmed Bacterial Infection	0	0	0	0

Gr3 Hematologic Toxicity Requiring Tx Delay...	0	0	0	0

End point values	Dose Determining Set: Phase 1: Nab-Paclitaxel 240 mg/m^2	Dose Determining Set: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	7		
Units: subjects				
At least 1 DLT	0	1		
Gr 3/4 Nonhematologic Toxicity...	0	0		
Gr 3/4 Nausea or Vomiting Persisting >5 days...	0	0		
Gr 4 Thrombocytopenia/Anemia Persisting >7 days...	0	0		
Gr 3 Thrombocytopenia with Bleeding	0	0		
Gr 4 Uncomplicated Neutropenia Lasting >7 days	0	1		
Febrile Neutropenia+Confirmed Bacterial Infection	0	0		
Gr3 Hematologic Toxicity Requiring Tx Delay...	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point title	Phase 1: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)[2][3]

End point description:

An adverse event (AE) was defined as any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study. A serious AE (SAE) is any AE occurring at any dose that: results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an important medical event. TEAEs were defined as AEs that began or worsened in severity on or after the date of the first dose of study drug and within 28 days of the date of the last dose of study drug. The severity of an AE was graded according to the CTCAE, Version 4.0.

Safety Population: all subjects who took at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Median treatment duration in Phase 1 was 7.0 weeks, with minimum and maximum duration of 1 and 49 weeks, respectively. Subjects were followed for 28 days after discontinuing treatment for safety and monitoring of AEs.

Notes:

[2] - 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: Endpoint data presented for Phase 1 only, per protocol.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint data presented for Phase 1 and Phase 2 presented separately.

End point values	Phase 1: Nab-Paclitaxel 120 mg/m^2	Phase 1: Nab-Paclitaxel 150 mg/m^2	Phase 1: Nab-Paclitaxel 180 mg/m^2	Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	8	14	11
Units: subjects				
TEAE	16	8	14	11
Treatment-related (TR) TEAE	14	8	12	11
Grade 3 or 4 TEAE	13	8	10	10
TR Grade 3 or 4 TEAE	9	7	7	9
Serious TEAE	10	7	6	5
TR Serious TEAE	1	4	4	2
TEAE Leading to IP Discontinuation	4	0	2	1
TR TEAE Leading to IP Discontinuation	1	0	0	1
TEAE Leading to Dose Reduction	0	1	2	1
TR TEAE Leading to Dose Reduction	0	1	2	1
TEAE Leading to IP Interruption	2	2	3	4
TR TEAE Leading to IP Interruption	0	2	1	3
TEAE Leading to Death	2	1	0	0
TR TEAE Leading to Death	0	0	0	0

End point values	Phase 1: Nab-Paclitaxel 240 mg/m^2	Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	7		
Units: subjects				
TEAE	8	7		
Treatment-related (TR) TEAE	7	7		
Grade 3 or 4 TEAE	8	7		
TR Grade 3 or 4 TEAE	7	7		
Serious TEAE	3	4		
TR Serious TEAE	1	3		
TEAE Leading to IP Discontinuation	2	2		
TR TEAE Leading to IP Discontinuation	2	2		
TEAE Leading to Dose Reduction	3	3		
TR TEAE Leading to Dose Reduction	3	3		
TEAE Leading to IP Interruption	3	2		
TR TEAE Leading to IP Interruption	3	2		
TEAE Leading to Death	1			

No statistical analyses for this end point

Primary: Phase 2: Overall Response Rate (ORR)

End point title	Phase 2: Overall Response Rate (ORR)[4]

End point description:

Overall response rate was defined as the percentage of subjects who achieved a complete response (CR; disappearance of all target lesions) or partial response (PR; at least a 30% decrease in the sum of diameters of target lesions) confirmed no less than 4 weeks after the criteria for response were first met using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 guidelines. (For Phase 2 neuroblastoma subjects who had both RECIST and Curie Score tumor evaluations, both tumor response results were considered and an overall response was derived.) Confidence interval was obtained using the Clopper-Pearson method.

End point type	Primary

End point timeframe:

Median treatment duration in Phase 2 per group: Ewings Sarcoma = 14 weeks (3-31), Neuroblastoma = 7 weeks (3-23), Rhabdomyosarcoma = 5 weeks (1-13).

Notes:

[4] - 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: Endpoint data presented for Phase 1 and Phase 2 separately.

End point values	Efficacy Evaluable Population: Phase 2: Ewing's Sarcoma	Efficacy Evaluable Population: Phase 2: Neuroblastoma	Efficacy Evaluable Population: Phase 2: Rhabdomyosarcoma	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	14	14	
Units: percentage of subjects				
number (confidence interval 95%)	0 (0.0 to 24.7)	0 (0.0 to 23.2)	7.1 (0.2 to 33.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: ORR

End point title	Phase 1: ORR

End point description:

Overall response rate was defined as the percentage of subjects who achieved a complete response (CR; disappearance of all target lesions) or partial response (PR: at least a 30% decrease in the sum of diameters of target lesions) confirmed no less than 4 weeks after the criteria for response were first met) using RECIST version 1.1 guidelines over the total number of subjects available for the analysis. Confidence interval was obtained using the Clopper-Pearson method.

End point type	Secondary

End point timeframe:

Median treatment duration in Phase 1 was 7.0 weeks, with minimum and maximum duration of 1 and 49 weeks, respectively.

End point values	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 120 mg/	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 150 mg/	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 180 mg/	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 210 mg/
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	8	12	10
Units: percentage of subjects				
number (confidence interval 95%)	0 (0.0 to 23.2)	0 (0.0 to 36.9)	0 (0.0 to 26.5)	0 (0.0 to 30.8)

End point values	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 240 mg/	Efficacy Evaluable Population: Phase 1: Nab-Paclitaxel 270 mg/		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	7		
Units: percentage of subjects				
number (confidence interval 95%)	12.5 (0.3 to 52.7)	14.3 (0.4 to 57.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Maximum Observed Concentration of Paclitaxel in Blood Plasma (Cmax)

End point title	Phase 1: Maximum Observed Concentration of Paclitaxel in Blood Plasma (Cmax)

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	7	12	9
Units: ng/mL				
geometric mean (geometric coefficient of variation)	3488 (± 73.7)	5468 (± 38.0)	5597 (± 33.4)	5616 (± 63.9)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	6		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	7831 (± 23.1)	8078 (± 41.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Cmax - Dose-Normalized

End point title	Phase 1: Cmax - Dose-Normalized

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	7	12	9
Units: ng/mL/[mg]				
geometric mean (geometric coefficient of variation)	23.3 (± 87.5)	25.4 (± 46.6)	27.3 (± 47.3)	23.2 (± 80.3)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	6		
Units: ng/mL/[mg]				
geometric mean (geometric coefficient	28.2 (± 48.7)	21.0 (± 46.6)		

of variation)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Area Under the Plasma Concentration-Time Curve (AUC)

End point title	Phase 1: Area Under the Plasma Concentration-Time Curve (AUC)

End point description:

Measurements include: AUC from time zero to the last measurable concentration (AUCt), AUC from time zero to 24 hours (AUC24), and AUC from time zero to infinity (AUCinf).

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13[5]	7[6]	12[7]	9[8]
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
AUCt; n=13, 7, 12, 9, 7, 6	7844 (± 73.4)	10374 (± 91.8)	9690 (± 37.1)	11817 (± 64.0)
AUC24; n=13, 7, 12, 8, 7, 6	6392 (± 79.0)	8944 (± 85.9)	8365 (± 37.7)	10932 (± 66.3)
AUCinf; n=9, 6, 10, 6, 6, 5	8867 (± 85.4)	11992 (± 99.8)	10087 (± 38.4)	14361 (± 72.1)

Notes:

[5] - n=subjects with an evaluable assessment for given measure

[6] - n=subjects with an evaluable assessment for given measure

[7] - n=subjects with an evaluable assessment for given measure

[8] - n=subjects with an evaluable assessment for given measure

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7[9]	6[10]		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
AUCt; n=13, 7, 12, 9, 7, 6	12706 (± 29.2)	11245 (± 22.6)		
AUC24; n=13, 7, 12, 8, 7, 6	11167 (± 27.4)	9768 (± 20.7)		

AUCinf; n=9, 6, 10, 6, 6, 5	14242 (± 29.2)	12424 (± 28.5)		

Notes:

[9] - n=subjects with an evaluable assessment for given measure

[10] - n=subjects with an evaluable assessment for given measure

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: AUC - Dose-Normalized

End point title	Phase 1: AUC - Dose-Normalized

End point description:

Measurements include: AUC24 and AUCinf.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13[11]	7[12]	12[13]	8[14]
Units: ng*h/mL/[mg]				
geometric mean (geometric coefficient of variation)				
AUC24; n=13, 7, 12, 8, 7, 6	42.7 (± 77.4)	41.6 (± 87.0)	40.8 (± 39.7)	43.3 (± 63.6)
AUCinf; n=9, 6, 10, 6, 6, 5	62.0 (± 75.7)	49.2 (± 101)	47.8 (± 39.8)	64.8 (± 25.4)

Notes:

[11] - n=subjects with an evaluable assessment for given measure

[12] - n=subjects with an evaluable assessment for given measure

[13] - n=subjects with an evaluable assessment for given measure

[14] - n=subjects with an evaluable assessment for given measure

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7[15]	6[16]		
Units: ng*h/mL/[mg]				
geometric mean (geometric coefficient of variation)				
AUC24; n=13, 7, 12, 8, 7, 6	40.2 (± 65.4)	25.4 (± 26.1)		
AUCinf; n=9, 6, 10, 6, 6, 5	52.3 (± 67.4)	31.3 (± 34.9)		

Notes:

[15] - n=subjects with an evaluable assessment for given measure

[16] - n=subjects with an evaluable assessment for given measure

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Clearance (CL)

End point title	Phase 1: Clearance (CL)

End point description:

Measurement of renal clearance from the body.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	6	10	6
Units: L/h				
geometric mean (geometric coefficient of variation)	16.1 (± 75.6)	20.3 (± 101)	20.9 (± 39.9)	15.4 (± 25.4)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	5		
Units: L/h				
geometric mean (geometric coefficient of variation)	19.1 (± 67.4)	31.9 (± 35.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: CL - Body Surface Area (BSA)-Normalized

End point title	Phase 1: CL - Body Surface Area (BSA)-Normalized
End point description:	
Measurement of renal clearance from the body.	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)	

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	6	10	6
Units: L/h/m^2				
geometric mean (geometric coefficient of variation)	13.5 (± 85.1)	12.5 (± 99.3)	17.8 (± 38.3)	14.6 (± 72.3)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	5		
Units: L/h/m^2				
geometric mean (geometric coefficient of variation)	16.7 (± 29.2)	21.8 (± 28.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Volume of Distribution (Vss)

End point title	Phase 1: Volume of Distribution (Vss)
End point description:	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)	

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	6	10	6
Units: liters				
geometric mean (geometric coefficient of variation)	127 (± 145)	266 (± 78.3)	146 (± 106)	89.8 (± 45.1)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	5		
Units: liters				
geometric mean (geometric coefficient of variation)	175 (± 117)	446 (± 17.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Vss - BSA-Normalized

End point title	Phase 1: Vss - BSA-Normalized

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects <6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 120 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 150 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 180 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	6	10	6
Units: L/m^2				
geometric mean (geometric coefficient of variation)	106 (± 95.3)	164 (± 78.4)	124 (± 82.8)	84.9 (± 49.7)

End point values	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 240 mg/m^2	Pharmacokinetic Population: Phase 1: Nab-Paclitaxel 270 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	5		
Units: L/m^2				
geometric mean (geometric coefficient of variation)	154 (± 56.5)	304 (± 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2 Population PK: Maximum Elimination Rate From the Central Compartment (VMEL)

End point title	Phase 1 and 2 Population PK: Maximum Elimination Rate From the Central Compartment (VMEL)

End point description:

Population PK analysis was performed using nonlinear mixed effect modeling. The estimated allometric function for VMEL was 1.12.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects < 6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: µg/h				
number (not applicable)	31983			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2 Population PK: Volume of Distribution of the Central Compartment (V1)

End point title	Phase 1 and 2 Population PK: Volume of Distribution of the Central Compartment (V1)

End point description:	
Population PK analysis was performed using nonlinear mixed effect modeling. The estimated allometric function for V1 was 0.888.	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects < 6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)	

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: liters				
number (not applicable)	11.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2 Population PK: Concentration in the Central Compartment at 50% of VMEL (KMEL)

End point title	Phase 1 and 2 Population PK: Concentration in the Central Compartment at 50% of VMEL (KMEL)
End point description:	
Population PK analysis was performed using nonlinear mixed effect modeling.	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects < 6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)	

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: µg/L				
number (not applicable)	951			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2 Population PK: Intercompartmental CL Between the

Central Compartment and the First Peripheral Compartment (Q2)	
End point title	Phase 1 and 2 Population PK: Intercompartmental CL Between the Central Compartment and the First Peripheral Compartment (Q2)
End point description:	
Population PK analysis was performed using nonlinear mixed effect modeling. The estimated allometric function for Q2 was 1.12.	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects < 6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)	

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: L/h				
number (not applicable)	22.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2 Population PK: Intercompartmental CL Between the Central Compartment and the Second Peripheral Compartment (Q3)	
End point title	Phase 1 and 2 Population PK: Intercompartmental CL Between the Central Compartment and the Second Peripheral Compartment (Q3)
End point description:	
Population PK analysis was performed using nonlinear mixed effect modeling. The estimated allometric function for Q3 was 1.12.	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects < 6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)	

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: L/h				
number (not applicable)				

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2 Population PK: Volume of Distribution of the First Peripheral Compartment (V2)

End point title	Phase 1 and 2 Population PK: Volume of Distribution of the First Peripheral Compartment (V2)

End point description:

Population PK analysis was performed using nonlinear mixed effect modeling. The estimated allometric function for V2 was 0.888.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects < 6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: liters				
number (not applicable)	545			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1 and 2 Population PK: Volume of Distribution of the Second Peripheral Compartment (V3)

End point title	Phase 1 and 2 Population PK: Volume of Distribution of the Second Peripheral Compartment (V3)

End point description:

Population PK analysis was performed using nonlinear mixed effect modeling. The estimated allometric function for V3 was 0.888.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Subjects ≥ 6 years: 1-2 minutes prior to the end of infusion [EOI], and 15 minutes, 1, 3, 5, 8, 24, 48, and 72 hours after the EOI. Subjects < 6 years: 1-2 minutes prior to the EOI, and 15 minutes, 3, 5, and 24 hours after the EOI.)

End point values	Pharmacokinetic Population			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: liters				
number (not applicable)	45.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response (DOR)

End point title	Phase 2: Duration of Response (DOR)

End point description:

Duration of response was defined as the time from the date of the first response (CR/PR, using RECIST version 1.1 guidelines) to disease progression for subjects with a confirmed CR or PR. Subjects who did not have disease progression or had not died were censored at the time of their last disease assessment or at time of start of new anticancer therapy, whichever occurred first. (For Phase 2 neuroblastoma subjects who had both RECIST version 1.1 and Curie Score tumor evaluations, both tumor responses results were considered and an overall response was derived.)

End point type	Secondary

End point timeframe:

Median treatment duration in Phase 2 per group: Ewings Sarcoma = 14 weeks (3-31), Neuroblastoma = 7 weeks (3-23), Rhabdomyosarcoma = 5 weeks (1-13). Subjects were followed until disease progression (if applicable) up to a maximum of 100.3 weeks.

End point values	Efficacy Evaluable Population: Phase 2: Ewing's Sarcoma	Efficacy Evaluable Population: Phase 2: Neuroblastoma	Efficacy Evaluable Population: Phase 2: Rhabdomyosarcoma	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[17]	0[18]	1	
Units: weeks				
median (full range (min-max))	(to)	(to)	6.14 (6.14 to 6.14)	

Notes:

[17] - no response in the Ewing's Sarcoma group

[18] - no response in the Neuroblastoma group

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Disease Control Rate (DCR)

End point title	Phase 2: Disease Control Rate (DCR)

End point description:

Disease control rate was defined as the percentage of subjects who achieved either a stable disease maintained for ≥ 16 weeks or confirmed CR (confirmed no less than 4 weeks after criteria for response were first met) or confirmed PR (confirmed no less than 4 weeks after criteria for response were first met) over the total number of subjects available for the analysis. Confidence interval was obtained using the Clopper-Pearson method.

End point type	Secondary

End point timeframe:

Median treatment duration in Phase 2 per group: Ewings Sarcoma = 14 weeks (3-31), Neuroblastoma = 7 weeks (3-23), Rhabdomyosarcoma = 5 weeks (1-13).

End point values	Efficacy Evaluable Population: Phase 2: Ewing's Sarcoma	Efficacy Evaluable Population: Phase 2: Neuroblastoma	Efficacy Evaluable Population: Phase 2: Rhabdomyosarcoma	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	14	14	
Units: percentage of subjects				
number (confidence interval 95%)	30.8 (9.1 to 61.4)	7.1 (0.2 to 33.9)	7.1 (0.2 to 33.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression-Free Survival (PFS)

End point title	Phase 2: Progression-Free Survival (PFS)

End point description:

PFS was defined as the time from the first dose date to the start of disease progression or subject death (any cause), whichever occurred first. Disease progression was classed as either a disease progression observed as a response assessment, or a disease progression or symptomatic deterioration at treatment/study discontinuation. Subjects who did not have disease progression or had not died were censored at the last known time that the subject was progression free. Disease progression was considered according to RECIST version 1.1 for Phase 2 Ewing's sarcoma and rhabdomyosarcoma subjects. (For Phase 2 neuroblastoma subjects who had both RECIST 1.1 and Curie score tumor evaluations, both tumor responses results were considered and an overall response was derived.) Median PFS time was estimated through Kaplan-Meier methods. 95% confidence interval about the median time to PFS event was obtained using Greenwood’s method.

End point type	Secondary

End point timeframe:

Median treatment duration in Phase 2 per group: Ewings Sarcoma = 14 weeks (3-31), Neuroblastoma = 7 weeks (3-23), Rhabdomyosarcoma = 5 weeks (1-13). Subjects were followed until disease progression (if applicable) up to a maximum of 100.3 weeks.

End point values	Efficacy Evaluable Population: Phase 2: Ewing's Sarcoma	Efficacy Evaluable Population: Phase 2: Neuroblastoma	Efficacy Evaluable Population: Phase 2: Rhabdomyosarcoma	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	14	14	
Units: weeks				
median (confidence interval 95%)	13 (7.4 to 16.1)	7.4 (4.6 to 8.1)	5.1 (2.1 to 7.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Kaplan-Meier Estimate of Overall Survival Rate at 1 year

End point title	Phase 2: Kaplan-Meier Estimate of Overall Survival Rate at 1 year

End point description:

Overall survival was defined as the time from the first dose date to date of death (any cause). Subjects who were alive were censored at the last known time that the subject was alive.

End point type	Secondary

End point timeframe:

1 year

End point values	Efficacy Evaluable Population: Phase 2: Ewing's Sarcoma	Efficacy Evaluable Population: Phase 2: Neuroblastoma	Efficacy Evaluable Population: Phase 2: Rhabdomyosarcoma	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	14	14	
Units: percentage of participants				
number (confidence interval 95%)	27 (7 to 53)	29 (9 to 52)	15 (2 to 39)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point title	Phase 2: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)[19]

End point description:

An AE was defined as any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study. A SAE is any AE occurring at any dose that: results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization;

results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect; constitutes an important medical event. TEAEs were defined as AEs that began or worsened in severity on or after the date of the first dose of study drug and within 28 days of the date of the last dose of study drug. The severity of the AEs was graded according to the Common Terminology Criteria for Adverse Events, Version 4.0. Subjects were followed for 28 days after discontinuing treatment for safety and monitoring of AEs.

Safety Population: all subjects who took at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Median treatment duration in Phase 2 for Ewings Sarcoma = 14 weeks (3-31), Neuroblastoma = 7 weeks (3-23), Rhabdomyosarcoma = 5 weeks (1-13); subjects were followed for 28 days after discontinuing treatment for safety and monitoring of AEs.

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint data presented for Phase 1 and Phase 2 separately.

End point values	Phase 2: Ewing's Sarcoma	Phase 2: Neuroblastoma	Phase 2: Rhabdomyosarcoma	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	14	14	
Units: Participants				
TEAE	14	14	14	
Treatment-related (TR) TEAE	13	12	12	
Grade 3 or 4 TEAE	12	13	12	
TR Grade 3 or 4 TEAE	9	9	10	
Serious TEAE	6	6	11	
TR Serious TEAE	2	2	6	
TEAE Leading to Drug Discontinuation	3	1	3	
TR TEAE Leading to Drug Discontinuation	1	0	3	
TEAE Leading to Dose Reduction	4	5	4	
TR TEAE Leading to Dose Reduction	4	4	4	
TEAE Leading to Drug Interruption	5	3	4	
TR TEAE Leading to Drug Interruption	3	3	2	
TEAE Leading to Death	0	2	3	
TR TEAE Leading to Death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects who Received at Least One Post-treatment Anticancer Therapy

End point title	Number of Subjects who Received at Least One Post-treatment Anticancer Therapy

End point description:

End point type	Other pre-specified

End point timeframe:

From the date of randomization to final date cut off date of 06 November 2018

End point values	Phase 1: Nab-Paclitaxel 120 mg/m^2	Phase 1: Nab-Paclitaxel 150 mg/m^2	Phase 1: Nab-Paclitaxel 180 mg/m^2	Phase 1: Nab-Paclitaxel 210 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	8	14	11
Units: subjects	12	2	12	10

End point values	Phase 1: Nab-Paclitaxel 240 mg/m^2	Phase 1: Nab-Paclitaxel 270 mg/m^2	Phase 2: Ewing's Sarcoma	Phase 2: Neuroblastoma
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	7	14	14
Units: subjects	7	6	11	9

End point values	Phase 2: Rhabdomyosarcoma			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: subjects	8			

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Median treatment duration in Phase 1 = 7.0 weeks (minimum and maximum duration of 1 and 49 weeks); median treatment duration in Phase 2 per group: Ewings sarcoma = 14 weeks (3-31), neuroblastoma = 7 weeks (3-23), rhabdomyosarcoma = 5 weeks (1-13).

Adverse event reporting additional description:

All subjects in both portions of the study were followed for 28 days after discontinuing treatment for safety and monitoring of AEs. AEs were analyzed in terms of TEAEs, which were defined as any AEs that began or worsened in severity on or after the start of study drug through 28 days after the last dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Phase 1: Nab-Paclitaxel 120 mg/m^2

Reporting group description:

nab-paclitaxel 120 mg/m^2 IV on Days 1, 8 and 15 of a 28- day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Reporting group title	Phase 1: Nab-paclitaxel 150 mg/m^2

Reporting group description:

nab-paclitaxel 150 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Reporting group title	Phase 1: Nab-paclitaxel 180 mg/m2

Reporting group description:

nab-paclitaxel 180 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Reporting group title	Phase 1: Nab-paclitaxel 210 mg/m2

Reporting group description:

nab-paclitaxel 210 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Reporting group title	Phase 1: Nab-paclitaxel 240 mg/m^2

Reporting group description:

nab-paclitaxel 240 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Reporting group title	Phase 1: Nab-paclitaxel 270 mg/m^2

Reporting group description:

nab-paclitaxel 270 mg/m^2 IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity to establish the RP2D.

Reporting group title	Phase 2: Sarcoma, Neuroblastoma and Rhabdomyosarcoma

Reporting group description:

Participants with Ewing's sarcoma, Neuroblastoma and Rhabdomyosarcoma received nab- paclitaxel at the RP2D (240 mg/m^2 in participants weighing > 10 kg and 11.5 mg/kg in participants weighing ≤ 10 kg) IV on Days 1, 8 and 15 of a 28-day cycle until disease progression, death, withdrawal of consent, or unacceptable toxicity.

Serious adverse events	Phase 1: Nab-Paclitaxel 120 mg/m^2	Phase 1: Nab-paclitaxel 150 mg/m^2	Phase 1: Nab-paclitaxel 180 mg/m2
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 16 (62.50%)	7 / 8 (87.50%)	6 / 14 (42.86%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteosarcoma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Osteosarcoma metastatic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Refractory anaemia with an excess of blasts			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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 disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Hypotension			

subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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 physical health deterioration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Generalised oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	3 / 8 (37.50%)	2 / 14 (14.29%)
occurrences causally related to treatment / all	0 / 0	6 / 8	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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
Hypoxia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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

Pleural effusion			
subjects affected / exposed	2 / 16 (12.50%)	0 / 8 (0.00%)	0 / 14 (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
Pneumonitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Pneumothorax			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Pulmonary embolism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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			
Anaphylactic transfusion reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Cardiac disorders			
Tachycardia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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
Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Intracranial pressure increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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
Seizure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Slow speech			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Somnolence			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Tremor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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
Neutropenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Dermatitis acneiform			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Dermatitis bullous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Erythema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Skin exfoliation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Anuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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
Urinary retention			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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
Urinary tract obstruction			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (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
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	2 / 16 (12.50%)	1 / 8 (12.50%)	0 / 14 (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
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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			
Cellulitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Device related infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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

Soft tissue infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Varicella			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (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
Hypercreatininaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	0 / 14 (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

Serious adverse events	Phase 1: Nab-paclitaxel 210 mg/m2	Phase 1: Nab-paclitaxel 240 mg/m^2	Phase 1: Nab-paclitaxel 270 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 11 (45.45%)	3 / 8 (37.50%)	4 / 7 (57.14%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Osteosarcoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Osteosarcoma metastatic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Refractory anaemia with an excess of blasts			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Tumour pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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			
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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			
Chills			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (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

General physical health deterioration			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (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
Generalised oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Pyrexia			
subjects affected / exposed	3 / 11 (27.27%)	1 / 8 (12.50%)	2 / 7 (28.57%)
occurrences causally related to treatment / all	7 / 8	0 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Hypoxia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Pneumonitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (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

Pneumothorax			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Injury, poisoning and procedural complications			
Anaphylactic transfusion reaction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Headache			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Intracranial pressure increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Seizure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (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
Slow speech			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Somnolence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Neutropenia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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			
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (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
Dermatitis bullous			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (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
Erythema			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Skin exfoliation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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			
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Anuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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 retention			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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 obstruction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Bone pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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

Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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			
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Device related infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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

Varicella			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Hypercreatininaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (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	Phase 2: Sarcoma, Neuroblastoma and Rhabdomyosarcoma		
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 42 (54.76%)		
number of deaths (all causes)	33		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteosarcoma			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteosarcoma metastatic			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Refractory anaemia with an excess of blasts			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 4		
Generalised oedema			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Oedema peripheral subjects affected / exposed	0 / 42 (0.00%)		

Respiratory failure			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Anaphylactic transfusion reaction			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Slow speech			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Somnolence			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dermatitis bullous			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erythema			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin exfoliation			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anuria			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Device related infection			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection bacterial			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hypercreatininaemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 1: Nab-Paclitaxel 120 mg/m^2	Phase 1: Nab-paclitaxel 150 mg/m^2	Phase 1: Nab-paclitaxel 180 mg/m2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	8 / 8 (100.00%)	14 / 14 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	4
Skin papilloma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tumour haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	2 / 16 (12.50%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	8	1	0
Vascular disorders			
Hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Hypotension			

subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	2 / 14 (14.29%)
occurrences (all)	0	1	2
Lymphoedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Catheter site pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 16 (18.75%)	3 / 8 (37.50%)	4 / 14 (28.57%)
occurrences (all)	5	6	5
General physical health deterioration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Generalised oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Influenza like illness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 16 (6.25%)	2 / 8 (25.00%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	0 / 14 (0.00%)
occurrences (all)	0	4	0
Oedema peripheral			

subjects affected / exposed	3 / 16 (18.75%)	3 / 8 (37.50%)	2 / 14 (14.29%)
occurrences (all)	4	11	2
Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	6 / 16 (37.50%)	3 / 8 (37.50%)	5 / 14 (35.71%)
occurrences (all)	17	3	8
Xerosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Genital pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Menstruation irregular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Oedema genital			
subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Scrotal oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	2 / 16 (12.50%)	3 / 8 (37.50%)	2 / 14 (14.29%)
occurrences (all)	4	8	2
Dysaesthesia pharynx			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	3 / 16 (18.75%)	0 / 8 (0.00%)	2 / 14 (14.29%)
occurrences (all)	3	0	3
Epistaxis			
subjects affected / exposed	1 / 16 (6.25%)	2 / 8 (25.00%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Haemoptysis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hypoxia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Lung consolidation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	0 / 14 (0.00%)
occurrences (all)	0	4	0
Pharyngeal erythema			
subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	1 / 14 (7.14%)
occurrences (all)	0	3	1
Pharyngeal inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pleural effusion			

subjects affected / exposed	2 / 16 (12.50%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Productive cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pulmonary haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 16 (12.50%)	3 / 8 (37.50%)	1 / 14 (7.14%)
occurrences (all)	2	3	1
Confusional state			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	1 / 16 (6.25%)	2 / 8 (25.00%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Enuresis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Mood altered			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Restless subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
Restless occurrences (all)	0	1	0
Investigations			
Activated partial thromboplastin time prolonged subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
Activated partial thromboplastin time prolonged occurrences (all)	1	1	0
Alanine aminotransferase increased subjects affected / exposed	0 / 16 (0.00%)	3 / 8 (37.50%)	1 / 14 (7.14%)
Alanine aminotransferase increased occurrences (all)	0	6	1
Aspartate aminotransferase increased subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	1 / 14 (7.14%)
Aspartate aminotransferase increased occurrences (all)	0	4	1
Blood alkaline phosphatase increased subjects affected / exposed	0 / 16 (0.00%)	4 / 8 (50.00%)	0 / 14 (0.00%)
Blood alkaline phosphatase increased occurrences (all)	0	9	0
Blood bicarbonate decreased subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
Blood bicarbonate decreased occurrences (all)	0	1	0
Blood bilirubin increased subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
Blood bilirubin increased occurrences (all)	1	2	0
Blood creatinine increased subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
Blood creatinine increased occurrences (all)	0	2	0
Blood lactate dehydrogenase increased subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
Blood lactate dehydrogenase increased occurrences (all)	0	0	1
Blood urea increased subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
Blood urea increased occurrences (all)	0	0	0
C-reactive protein increased subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
C-reactive protein increased occurrences (all)	0	0	0
Candida test positive			

subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)

Arthropod bite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Recall phenomenon			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Scar			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Vascular access complication			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Wound secretion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Aortic valve disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pericardial effusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Sinus bradycardia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)	2 / 8 (25.00%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Dysaesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	3 / 16 (18.75%)	2 / 8 (25.00%)	3 / 14 (21.43%)
occurrences (all)	4	7	4
Lethargy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
Neuralgia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	3
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	1	4	1
Spinal cord compression			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Visual field defect			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 16 (50.00%)	6 / 8 (75.00%)	6 / 14 (42.86%)
occurrences (all)	17	19	20
Febrile neutropenia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	6 / 16 (37.50%)	1 / 8 (12.50%)	2 / 14 (14.29%)
occurrences (all)	22	20	15
Lymphadenitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	6 / 16 (37.50%)	2 / 8 (25.00%)	1 / 14 (7.14%)
occurrences (all)	15	5	5
Neutropenia			
subjects affected / exposed	7 / 16 (43.75%)	4 / 8 (50.00%)	6 / 14 (42.86%)
occurrences (all)	22	24	27
Neutrophilia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 16 (6.25%)	2 / 8 (25.00%)	2 / 14 (14.29%)
occurrences (all)	3	4	3
Thrombocytosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Ear swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Diplopia			

subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Keratitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	2 / 16 (12.50%)	2 / 8 (25.00%)	3 / 14 (21.43%)
occurrences (all)	4	6	3

Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	2 / 14 (14.29%)
occurrences (all)	0	1	2
Anal fissure			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Anal incontinence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Anal inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Anorectal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	4 / 16 (25.00%)	3 / 8 (37.50%)	3 / 14 (21.43%)
occurrences (all)	4	4	4
Diarrhoea			
subjects affected / exposed	2 / 16 (12.50%)	4 / 8 (50.00%)	4 / 14 (28.57%)
occurrences (all)	2	8	14
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 8 (25.00%)	1 / 14 (7.14%)
occurrences (all)	0	5	1
Eructation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	3

Gastrointestinal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	6 / 16 (37.50%)	3 / 8 (37.50%)	2 / 14 (14.29%)
occurrences (all)	6	9	2
Odynophagia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Toothache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	0	3	1
Vomiting			
subjects affected / exposed	8 / 16 (50.00%)	3 / 8 (37.50%)	2 / 14 (14.29%)
occurrences (all)	10	14	6
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	2 / 16 (12.50%)	4 / 8 (50.00%)	4 / 14 (28.57%)
occurrences (all)	2	5	5
Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Dermatitis atopic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Intertrigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nail bed inflammation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nail discolouration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Onycholysis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pain of skin			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Photosensitivity reaction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)	2 / 8 (25.00%)	0 / 14 (0.00%)
occurrences (all)	2	7	0
Pruritus generalised			
subjects affected / exposed	3 / 16 (18.75%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	1
Rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			

subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Skin hyperpigmentation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Toxic erythema of chemotherapy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	4	0
Dysuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Ketonuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Polyuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Renal pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	0	1	1

Urinary tract obstruction			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Urinary tract pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	2 / 16 (12.50%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	2	1	2
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	4 / 8 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	4	0
Neck pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	2 / 16 (12.50%)	3 / 8 (37.50%)	2 / 14 (14.29%)
occurrences (all)	2	3	2
Pain in jaw			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Clostridium difficile infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Cystitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Device related infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Ear infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Lung infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Mucosal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Rash pustular			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	0	1	2
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	2 / 14 (14.29%)
occurrences (all)	0	3	3
Skin infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 16 (12.50%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	3	0	1
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	4	0
Cachexia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	3 / 16 (18.75%)	3 / 8 (37.50%)	5 / 14 (35.71%)
occurrences (all)	4	4	5
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hyperchloraemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Hypercreatininaemia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Hyperglycaemia			
subjects affected / exposed	2 / 16 (12.50%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	2	6	0
Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	4	0
Hypermagnesaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 16 (12.50%)	3 / 8 (37.50%)	0 / 14 (0.00%)
occurrences (all)	2	7	0
Hypocalcaemia			
subjects affected / exposed	2 / 16 (12.50%)	2 / 8 (25.00%)	1 / 14 (7.14%)
occurrences (all)	3	9	2
Hypochloraemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 8 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	1 / 16 (6.25%)	3 / 8 (37.50%)	2 / 14 (14.29%)
occurrences (all)	1	12	2
Hypomagnesaemia			

subjects affected / exposed	1 / 16 (6.25%)	1 / 8 (12.50%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Hyponatraemia			
subjects affected / exposed	1 / 16 (6.25%)	4 / 8 (50.00%)	1 / 14 (7.14%)
occurrences (all)	1	13	1
Hypophosphataemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 8 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Polydipsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 8 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1

Non-serious adverse events	Phase 1: Nab-paclitaxel 210 mg/m2	Phase 1: Nab-paclitaxel 240 mg/m^2	Phase 1: Nab-paclitaxel 270 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	8 / 8 (100.00%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin papilloma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tumour haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	3	0	1
Vascular disorders			
Hyperaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Hypotension			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 11 (9.09%)	3 / 8 (37.50%)	1 / 7 (14.29%)
occurrences (all)	1	5	2
Catheter site pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	4 / 11 (36.36%)	2 / 8 (25.00%)	0 / 7 (0.00%)
occurrences (all)	8	2	0
General physical health deterioration			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Generalised oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	5 / 11 (45.45%)	4 / 8 (50.00%)	2 / 7 (28.57%)
occurrences (all)	15	11	6
Xerosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Genital pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Oedema genital			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Scrotal oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal discomfort			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cough			

subjects affected / exposed	4 / 11 (36.36%)	3 / 8 (37.50%)	0 / 7 (0.00%)
occurrences (all)	4	3	0
Dysaesthesia pharynx			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Haemoptysis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Lung consolidation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pharyngeal erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pharyngeal inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Enuresis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Mood altered			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Restlessness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 11 (27.27%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	4	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	2 / 11 (18.18%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Candida test positive			

subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Electroencephalogram abnormal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

0 / 7 (0.00%)
subjects affected / exposed

Arthropod bite			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Excoriation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 11 (0.00%)	2 / 8 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Humerus fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Muscle injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Recall phenomenon			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Scar			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	3
Vascular access complication			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Wound secretion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			

Aortic valve disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Dysgeusia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	2
Headache			
subjects affected / exposed	2 / 11 (18.18%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	2	1	2
Lethargy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neuralgia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	0	1	2
Peripheral motor neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	2 / 8 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	3 / 8 (37.50%)	2 / 7 (28.57%)
occurrences (all)	0	7	4
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Visual field defect			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 11 (45.45%)	6 / 8 (75.00%)	6 / 7 (85.71%)
occurrences (all)	15	13	25
Febrile neutropenia			

subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	5 / 11 (45.45%)	5 / 8 (62.50%)	3 / 7 (42.86%)
occurrences (all)	9	38	34
Lymphadenitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	2 / 11 (18.18%)	2 / 8 (25.00%)	3 / 7 (42.86%)
occurrences (all)	5	9	27
Neutropenia			
subjects affected / exposed	8 / 11 (72.73%)	7 / 8 (87.50%)	6 / 7 (85.71%)
occurrences (all)	33	43	38
Neutrophilia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 8 (25.00%)	4 / 7 (57.14%)
occurrences (all)	3	6	11
Thrombocytosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Eye disorders			
Diplopia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Eye irritation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Eye pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	2 / 11 (18.18%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	2
Photophobia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	2 / 11 (18.18%)	3 / 8 (37.50%)	2 / 7 (28.57%)
occurrences (all)	2	6	6

Abdominal pain upper			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Anal fissure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Anorectal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	6 / 11 (54.55%)	2 / 8 (25.00%)	1 / 7 (14.29%)
occurrences (all)	8	2	1
Diarrhoea			
subjects affected / exposed	3 / 11 (27.27%)	4 / 8 (50.00%)	2 / 7 (28.57%)
occurrences (all)	6	5	7
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 8 (25.00%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Eructation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	4 / 11 (36.36%)	2 / 8 (25.00%)	3 / 7 (42.86%)
occurrences (all)	6	4	6
Odynophagia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	2 / 11 (18.18%)	1 / 8 (12.50%)	2 / 7 (28.57%)
occurrences (all)	3	1	2
Toothache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	3 / 11 (27.27%)	3 / 8 (37.50%)	1 / 7 (14.29%)
occurrences (all)	6	6	3
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	5 / 11 (45.45%)	3 / 8 (37.50%)	2 / 7 (28.57%)
occurrences (all)	9	4	3
Dermatitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dermatitis atopic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	2 / 11 (18.18%)	2 / 8 (25.00%)	2 / 7 (28.57%)
occurrences (all)	2	2	2
Ecchymosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Erythema			
subjects affected / exposed	2 / 11 (18.18%)	2 / 8 (25.00%)	1 / 7 (14.29%)
occurrences (all)	3	2	1
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Intertrigo			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nail bed inflammation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nail discolouration			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Onychoclasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Onycholysis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	7
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	3
Photosensitivity reaction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
Pruritus generalised			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Rash			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Rash erythematous			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	5	0	1
Rash macular			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	3	1	8
Rash maculo-papular			
subjects affected / exposed	0 / 11 (0.00%)	2 / 8 (25.00%)	1 / 7 (14.29%)
occurrences (all)	0	5	1
Rash papular			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation			

subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin hyperpigmentation			
subjects affected / exposed	1 / 11 (9.09%)	2 / 8 (25.00%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Toxic erythema of chemotherapy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	4
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Ketonuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Polyuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Urinary tract obstruction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Urinary tract pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 11 (36.36%)	2 / 8 (25.00%)	2 / 7 (28.57%)
occurrences (all)	7	3	4
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	2 / 8 (25.00%)	0 / 7 (0.00%)
		4	

subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	3 / 8 (37.50%)	1 / 7 (14.29%)
occurrences (all)	0	4	1
Pain in jaw			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Cystitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Device related infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Mucosal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Rash pustular			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Skin infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Vulvitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	3
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cachexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	1	1	3
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperchloraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypercreatininaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 8 (12.50%)	2 / 7 (28.57%)
occurrences (all)	1	1	2
Hypomagnesaemia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Polydipsia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2: Sarcoma, Neuroblastoma and Rhabdomyosarcoma		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Skin papilloma			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Tumour haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Tumour pain			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Vascular disorders			
Hyperaemia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Hypertension			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypotension			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Lymphoedema			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	9		
Catheter site pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Face oedema			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
General physical health deterioration			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Generalised oedema			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Oedema peripheral			

subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	11		
Pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	14 / 42 (33.33%)		
occurrences (all)	26		
Xerosis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Genital pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Menstruation irregular			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Oedema genital			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Scrotal oedema			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Vulvovaginal discomfort			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	10		
Dysaesthesia pharynx			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	8		
Haemoptysis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypoxia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Lung consolidation			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pharyngeal erythema			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pharyngeal inflammation			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pleural effusion			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pulmonary haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Tachypnoea			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Enuresis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Mood altered			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		

Restlessness			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	5		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Blood bicarbonate decreased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Blood urea increased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Candida test positive			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Electroencephalogram abnormal			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Glucose urine present			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
International normalised ratio increased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Platelet count decreased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Urine output decreased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			

Arthropod bite				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Contusion				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Excoriation				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			

Aortic valve disease			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pericardial effusion			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Sinus bradycardia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Dysaesthesia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	15		
Lethargy			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Neuralgia			

subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	7		
Neuropathy peripheral			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Peripheral motor neuropathy			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	8		
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Spinal cord compression			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Visual field defect			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	27 / 42 (64.29%)		
occurrences (all)	68		
Febrile neutropenia			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	18 / 42 (42.86%)		
occurrences (all)	69		
Lymphadenitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	10		
Neutropenia			
subjects affected / exposed	23 / 42 (54.76%)		
occurrences (all)	97		
Neutrophilia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	37		
Thrombocytosis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Ear swelling			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Eye disorders			
Diplopia			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dry eye			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Eye irritation			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Eye pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Eye pruritus			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Keratitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Lacrimation increased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Periorbital oedema			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Photophobia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	9		

Abdominal pain upper			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Anal fissure			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Anal incontinence			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Anal inflammation			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Anorectal discomfort			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Ascites			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	12		
Diarrhoea			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	11		
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Eructation			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		

Gastrointestinal pain subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Haematochezia subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Haemorrhoids subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	 10 / 42 (23.81%) 12		
Odynophagia subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Salivary hypersecretion subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Stomatitis subjects affected / exposed occurrences (all)	 8 / 42 (19.05%) 9		
Toothache subjects affected / exposed occurrences (all)	 2 / 42 (4.76%) 2		
Vomiting subjects affected / exposed occurrences (all)	 14 / 42 (33.33%) 22		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	8		
Dermatitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dermatitis atopic			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Ecchymosis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	8		
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Intertrigo			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Nail bed inflammation			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Nail discolouration			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Onychoclasis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		

Onycholysis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pain of skin			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	4		
Photosensitivity reaction			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Pruritus			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Pruritus generalised			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Rash			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Rash erythematous			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rash macular			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	10		
Rash papular			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Skin exfoliation			

subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Skin hyperpigmentation			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Toxic erythema of chemotherapy			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Haematuria			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Ketonuria			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Polyuria			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Renal pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		

Urinary tract obstruction			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Urinary tract pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Coccydynia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Epiphysiolysis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Muscular weakness			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	17 / 42 (40.48%)		
occurrences (all)	23		
Pain in jaw			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Spinal pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Clostridium difficile infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		

Cystitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Device related infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)			

Rash pustular			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Vulvitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Cachexia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Dehydration			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hyperchloraemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypercreatininaemia			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypermagnesaemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypernatraemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	4		
Hypocalcaemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypochloraemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Hypomagnesaemia			

subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	4		
Hyponatraemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Polydipsia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2013	1. A global administrative change of sponsor name from 'Abraxis BioScience, LLC, a wholly-owned subsidiary of Celgene Corporation' to 'Celgene Corporation' to reflect the retirement of the legacy entity 'Abraxis BioScience, LLC, a wholly-owned subsidiary of Celgene Corporation' as sponsor name. 2. The addition of echocardiogram/MUGA scans for increased cardiotoxicity monitoring. 3. Modification of the schedule of events to increase the frequency of 12-lead ECG testing. 4. The addition of a 3-month washout period for HSCT to the exclusion criteria. 5. A decrease in the volume of blood drawn for PK sampling. 6. An administrative change to clarify the PK sampling requirements for samples collected up to 1 hour after the end of study drug infusion. 7. Removal of Cycle 1 Day 1 urine homovanillic acid and vanillylmandelic acid testing. 8. Clarification and updates in the statistical analysis section (eg, safety analysis). 9. An administrative change to include the use of IRT for patient enrollment • Addition of company standard language for End of Trial, overdose, Adverse Events, Serious Adverse Events, pregnancy language, site responsibilities and monitoring, and administrative procedures • Administrative changes to correct minor errors and inconsistencies within the document and/or case report forms
12 March 2014	1. In the Phase 2 portion, a change to the sample size for the Phase 2 neuroblastoma arm, and modifications of the Simon two-stage minimax design to implement acceptance rates of approximately 20% response rates for the neuroblastoma and rhabdomyosarcoma arms. 2. The addition of ≥ Grade 2 peripheral neuropathy to the exclusion criteria. 3. The addition of information concerning the use of syringe-based devices for administration of small volumes of nab-paclitaxel suspension. 4. A change from cautionary use to prohibition of concomitant medications classified as strong inducers of CYP2C8 and CYP3A4, and additional guidance on the use of strong inhibitors of the same isozymes. 5. An administrative change to the Medical Monitor title and contact information. 6. An administrative change to include the approval of nab-paclitaxel in the US and EU for the treatment of first-line metastatic pancreatic adenocarcinoma. 7. Clarification and updates to the description of the rolling-6 design for the Phase 1 portion. 8. The addition of the use of "other medically appropriate method" for LVSF assessment. 9. The addition of company standard language for the description of investigational product. 10. Clarification of permitted dose reductions from dose level -1 in the Phase 1 portion. 11. Clarification of recommendation concerning labeling of PK samples. 12. Administrative changes to clarify protocol language and provide one additional literature reference. 13. Administrative changes to correct minor formatting errors.
11 June 2014	Significant changes included in this amendment are summarized below: 1. Update to the new IND number for nab-paclitaxel for the pediatric solid tumors indication. 2. Add specific language to discontinue and not rechallenge treatment for hypersensitivity as agreed with the FDA. 3. Clarify with specific language to discontinue treatment at the third recurrence for neutropenia events as agreed with the FDA.

25 March 2015	1. Increased scope of dense PK sample collection 2. Change of the third solid tumors group in Phase (Ph) 2 from mixed tumors to Ewing's sarcoma 3. Harmonization of sample size and Simon two-stage minimax design for the 3 groups in Ph 2 4. Updated inclusion 2 for Ph 2 requiring radiologically documented measurable disease by RECIST version 1.1 (for neuroblastoma evaluable disease by MIBG/Curie Score 5. Updated assessment of the primary endpoint ORR in the Ph 2 neuroblastoma group to use both the RECIST version 1.1 criteria and the Curie score 6. Confirmation of CR in Ph 2 neuroblastoma 7. Decreased minimum platelet level in inclusion 5 for Ph 2 with known bone marrow involvement 8. Addition of guidance on flushing the IV line following infusion of nab-paclitaxel 9. Addition of statements regarding study conduct in compliance with ICH GCPs to align with company standard protocol language 10. Clarification of Ph 1 sample size to: additional patients enrolled at dose levels evaluated as safe by the SMC. 11. Update to length of Ph 1 (from 12 months to up to 18 months) 12. Clarification of SAE reporting during the 28-day follow-up to align with updated company standard protocol language 13. Update to the description of response assessments to include that the sponsor may conduct an independent assessment of response after study completion 14. Update to inclusion 8 to align with current Celgene Standard Risk Language 15. Clarification of safety analysis:I include summarization of AEs of special interest 16. Update to treatment discontinuation information concerning the treating physician's responsibilities 17. Update to align with company standard protocol language concerning investigator responsibilities for handling of confidential information 18. Update to align with company standard protocol language concerning publication 19. Addition of references 20. Clarification that the MIBG tumor response assessment includes a 10th segment for any soft tissue involvement
13 July 2016	Significant changes included in this amendment are summarized below: 1. Updated inclusion criterion 1b for Phase 2 to allow enrollment of patients ≥ 6 months to ≤ 24 years of age. 2. Updated inclusion criterion 2b for Phase 2 to allow enrollment of patients who have failed up to three lines of treatment. 3. Modification of exclusion criterion 7 to differentiate between autologous and allogeneic HSCT. 4. Updated assessment of the primary endpoint (ORR) in the Phase 2 neuroblastoma group using both RECIST version 1.1 criteria and the Curie score. 5. Clarification of definition of the efficacy evaluable population 6. Addition of definition of nab-paclitaxel overdose 7. Identification of the RP2D 8. Updated Phase 1 enrollment numbers 9. Allowance for the use of historical LVSF assessments and ECGs at Screening

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported