Clinical trial results:
Phase 1/2 Study of Lenvatinib in Children and Adolescents With Refractory or Relapsed Solid Malignancies and Young Adults with Osteosarcoma

Summary

EudraCT number	2013-005534-38
Trial protocol	GB ES DE FR IT Outside EU/EEA
Global end of trial date	20 July 2022

Results information

Result version number	v1 (current)
This version publication date	21 January 2023
First version publication date	21 January 2023

Trial information

Trial identification

Sponsor protocol code	E7080-G000-207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02432274
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Ltd.
Sponsor organisation address	Mosquito Way, Hatfield, Hertfordshire, United Kingdom, AL10 9SN
Public contact	Eisai Medical Information, Eisai Ltd., +1 888-274-2378, esi_oncmedinfo@eisai.com
Scientific contact	Eisai Medical Information, Eisai Ltd., +1 888-274-2378, esi_oncmedinfo@eisai.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001119-PIP02-12
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Cohort 1 (Single-agent Dose-Finding) -Identify the recommended dose (RD) of lenvatinib as a single agent in children and adolescents with relapsed or refractory solid malignant tumors. Cohort 2 (Single-agent Expansion) -Evaluate the activity of lenvatinib in 2 separate malignancy groups: Cohort 2A: 131 iodine- refractory differentiated thyroid cancer (DTC): by objective response rate (ORR) for subjects with measurable disease and by best overall response (BOR) for all subjects. Cohort 2B: Relapsed or refractory osteosarcoma: by progression-free survival at 4 months (PFS)-4. Cohort 3 (Combination Dose-Finding and Expansion) Cohort 3A (Combination Dose-Finding) -To identify the RD of lenvatinib in combination with ifosfamide and etoposide in osteosarcoma subjects. Cohort 3B (Combination Expansion) -Evaluate the activity of lenvatinib in combination with ifosfamide and etoposide in osteosarcoma subjects by PFS-4.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following: - Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008) - International Conference on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use - Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312 - European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states. - Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan’s GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 December 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	France: 34
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Italy: 18

Worldwide total number of subjects	97
EEA total number of subjects	71

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	20
Adolescents (12-17 years)	60
Adults (18-64 years)	17
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part at 19 investigative sites in France, Germany, Italy, Spain, United Kingdom and the United States. Total 117 subjects were enrolled and screened, of which 20 subjects were screen failures and 97 subjects received study treatment.

Pre-assignment

Screening details:

Prior to entering Cohort 1, subjects aged 2 to less than (<) 6 years underwent a run-in period and received lenvatinib 5 milligram per square meter (mg/m^2) per body surface area (BSA) as capsules or suspension once daily for 21 days.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2

Arm description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 11 mg/m^2 (administered per body surface area[BSA]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by the sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 11 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining recommended dose (RD) in Cohort 1,subjects were enrolled in Cohorts 2A, 2B and 3A.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib 11 mg/m^2, capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28. 2 subjects from arm Cohort 1 lenvatinib 17 mg/m^2 actually received lenvatinib 11 mg/m^2.

Arm title	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2

Arm description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 14 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by the sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 14 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Arm type	Experimental

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib 14 mg/m^2, capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28. 2 subjects from arm Cohort 1 lenvatinib 17 mg/m^2 actually received lenvatinib 14 mg/m^2.

Arm title	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2

Arm description:

Subjects (of age group 6 to <18 years) with relapsed or refractory solid malignant tumors received dose of lenvatinib 17 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each cycle in Cohort 1=28 days. After determining the RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib 17 mg/m^2, capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28.

Arm title	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2

Arm description:

Subjects with 131 iodine-refractory differentiated thyroid cancer (DTC) received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 milligram per day [mg/day]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2A=28 days.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib 14 mg/m^2, capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28.

Arm title	Cohort2B,SingleagentExpansion, Osteosarcoma:Lenvatinib14mg/m^2

Arm description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 mg/day) as capsule or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another

anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2B=28 days.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib 14 mg/m^2, capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28.

Arm title	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2

Arm description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 11 mg/m^2 (20 percent [%] lower than the recommended dose from Cohort 1; administered per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 milligram per square meter per day (mg/m^2/day) intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib 11 mg/m^2, capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21. 4 subjects from arm Cohort 3A lenvatinib 14 mg/m^2 actually received lenvatinib 11 mg/m^2.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Etoposide 100 mg/m^2/day, intravenous infusion, once daily on Days 1 to 3.

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Ifosfamide 3000 mg/m^2/day, intravenous infusion, once daily on Days 1 to 3.

Arm title	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2

Arm description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received Lenvatinib 14 mg/m^2, capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21.

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Ifosfamide 3000 mg/m^2/day, intravenous infusion, once daily on Days 1 to 3.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Etoposide 100 mg/m^2/day, intravenous infusion, once daily on Days 1 to 3.

Arm title	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2

Arm description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3B=21 days.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received Lenvatinib 14 mg/m^2, capsule or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21.

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Ifosfamide 3000 mg/m^2/day, intravenous infusion, once daily on Days 1 to 3.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion

Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Etoposide 100 mg/m^2/day, intravenous infusion, once daily on Days 1 to 3.

Number of subjects in period 1	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2
Started	3	9	11
Underwent Run-in Period	1	1 [1]	0 [2]
Completed	1	3	4
Not completed	2	6	7
Consent withdrawn by subject	-	-	-
Death	2	6	7

Number of subjects in period 1	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2	Cohort2B,SingleagentExpansion, Osteosarcoma:Lenvatinib14mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2
Started	1	31	7
Underwent Run-in Period	0 [3]	0 [4]	0
Completed	1	2	0
Not completed	0	29	7
Consent withdrawn by subject	-	2	-
Death	-	27	7

Number of subjects in period 1	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Started	15	20
Underwent Run-in Period	0 [5]	0 [6]
Completed	5	4
Not completed	10	16
Consent withdrawn by subject	1	2
Death	9	14

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone signifies subjects who were exclusively assigned to run-in period from respective arms.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the

arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone signifies subjects who were exclusively assigned to run-in period from respective arms.
[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone signifies subjects who were exclusively assigned to run-in period from respective arms.
[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone signifies subjects who were exclusively assigned to run-in period from respective arms.
[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone signifies subjects who were exclusively assigned to run-in period from respective arms.
[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone signifies subjects who were exclusively assigned to run-in period from respective arms.

Reporting groups

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2

Reporting group description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 11 mg/m^2 (administered per body surface area[BSA]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by the sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 11 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining recommended dose (RD) in Cohort 1,subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 14 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by the sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 14 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2

Reporting group description:

Subjects (of age group 6 to <18 years) with relapsed or refractory solid malignant tumors received dose of lenvatinib 17 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each cycle in Cohort 1=28 days. After determining the RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with 131 iodine-refractory differentiated thyroid cancer (DTC) received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 milligram per day [mg/day]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2A=28 days.

Reporting group title	Cohort2B,SingleagentExpansion, Osteosarcoma:Lenvatinib14mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 mg/day) as capsule or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2B=28 days.

Reporting group title	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 11 mg/m^2 (20 percent [%] lower than the recommended dose from Cohort 1; administered per BSA with daily dose capped at 24

mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 milligram per square meter per day (mg/m^2/day) intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Reporting group title	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Reporting group title	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3B=21 days.

Reporting group values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2
Number of subjects	3	9	11
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	1	4	5
Adolescents (12-17 years)	2	5	6
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	10.7	11.4	12.0
standard deviation	± 7.09	± 4.80	± 3.35
Gender categorical Units: Subjects			
Female	1	5	5
Male	2	4	6
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	1	4	4
Unknown or Not Reported	1	4	5

Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	5	3
More than one race	0	0	1
Unknown or Not Reported	1	4	7

Reporting group values	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2	Cohort2B,SingleagentExpansion, Osteosarcoma:Lenvatinib14mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2
Number of subjects	1	31	7
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	4	1
Adolescents (12-17 years)	1	20	4
Adults (18-64 years)	0	7	2
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	17.0	14.9	15.1
standard deviation	± 17.0	± 3.27	± 3.63
Gender categorical Units: Subjects			
Female	0	18	2
Male	1	13	5
Ethnicity Units: Subjects			
Hispanic or Latino	0	4	1
Not Hispanic or Latino	0	15	5
Unknown or Not Reported	1	12	1
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	1	20	6
More than one race	0	2	0
Unknown or Not Reported	0	9	1

Reporting group values	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2	Total
Number of subjects	15	20	97
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	3	2	20
Adolescents (12-17 years)	9	13	60
Adults (18-64 years)	3	5	17
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	14.2	15.8	
standard deviation	± 4.74	± 4.05	-
Gender categorical Units: Subjects			
Female	5	7	43
Male	10	13	54
Ethnicity Units: Subjects			
Hispanic or Latino	4	3	16
Not Hispanic or Latino	8	10	47
Unknown or Not Reported	3	7	34
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	14	13	64
More than one race	0	3	6
Unknown or Not Reported	1	4	27

End points reporting groups

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2

Reporting group description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 11 mg/m^2 (administered per body surface area[BSA]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by the sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 11 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining recommended dose (RD) in Cohort 1,subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 14 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by the sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 14 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2

Reporting group description:

Subjects (of age group 6 to <18 years) with relapsed or refractory solid malignant tumors received dose of lenvatinib 17 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each cycle in Cohort 1=28 days. After determining the RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with 131 iodine-refractory differentiated thyroid cancer (DTC) received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 milligram per day [mg/day]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2A=28 days.

Reporting group title	Cohort2B,SingleagentExpansion, Osteosarcoma:Lenvatinib14mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 mg/day) as capsule or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2B=28 days.

Reporting group title	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 11 mg/m^2 (20 percent [%] lower than the recommended dose from Cohort 1; administered per BSA with daily dose capped at 24

mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 milligram per square meter per day (mg/m^2/day) intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Reporting group title	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Reporting group title	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3B=21 days.

Subject analysis set title	Cohort 1: All Subjects
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects (of age group 2 to <6 years [following the completion of run-in period] and 6 to <18 years) with relapsed or refractory solid malignant tumors received dose of lenvatinib 11 mg/m^2, 14 mg/m^2 or 17 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each cycle in Cohort 1=28 days.

Subject analysis set title	Cohort 3A: All Subjects
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 11 mg/m^2 (20% lower than the recommended dose from Cohort 1) or 14 mg/m^2, administered per BSA with daily dose capped at 24 mg/day as capsule or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as lenvatinib suspension), orally, once daily on Days 1 to 21 of each treatment cycle, in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as combination therapy. Duration of each cycle=21 days.

Subject analysis set title	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects (of age group 2 to <6 years and 6 to <18 years)with relapsed or refractory solid malignant tumors received lenvatinib 11 mg/m^2(administered per body surface area[BSA])as capsules or suspension(lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension),orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by sponsor, whichever occurred first. Eligible subject of age group 2 to <6 years first underwent 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 11 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining RD in Cohort 1, subjects were enrolled in Cohorts 2A,2B and 3A.

Subject analysis set title	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 14 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib

capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 14 mg/m^2 in Cycle 1 in Cohort 1. Duration of each treatment cycle in Cohort 1=28 days. After determining RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Subject analysis set title	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects (of age group 6 to <18 years) with relapsed or refractory solid malignant tumors received dose of lenvatinib 17 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each cycle in Cohort 1=28 days. After determining the RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Subject analysis set title	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects with 131 iodine-refractory differentiated thyroid cancer (DTC) received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 milligram per day [mg/day]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2A=28 days.

Subject analysis set title	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 mg/day) as capsule or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each treatment cycle in Cohort 2B=28 days.

Subject analysis set title	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 11 mg/m^2 (20 percent [%] lower than the recommended dose from Cohort 1; administered per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 milligram per square meter per day (mg/m^2/day) intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Subject analysis set title	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Subject analysis set title	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3B=21 days.

Primary: Cohort 1: Recommended Dose (RD) of Lenvatinib

End point title	Cohort 1: Recommended Dose (RD) of Lenvatinib[1]

End point description:

RD:dose that had dose limiting toxicity(DLT)rate closest to 20% rate.DLT:adverse drug reaction and assessed according to common terminology criteria for adverse events(CTCAE)version (v) 4.03 defined as 1) Grade4 neutropenia for greater than or equal to(>=)7 days,2) Grade>=3 thrombocytopenia with bleeding,or lasting greater than(>)7 days,3)Grade>=3 febrile neutropenia,4) Next course chemotherapy delayed>=7 days,5) Grade>=3 nonhematologic toxicity persisting >7 days optimal supportive care,6) Grade 4 hypertension,confirmed systolic/diastolic blood pressure>25 millimeters of mercury(mmHg)above 95th percentile for age, or elevated diastolic blood pressure(>95th percentile for age)not controlled by single antihypertensive medication within 14 days use,7) Grade3 proteinuria,8) Any recurrent Grade2 nonhematological toxicity requiring>=2 interruption and dose reductions.Safety analysis set included all subjects who received any study drug and had at least one post-baseline safety evaluation.

End point type	Primary

End point timeframe:

Cycle 1 (28 days)

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: No statistical analysis was planned for this endpoint.

End point values	Cohort 1: All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: milligram per meter square (mg/m^2)				
number (not applicable)	14			

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 2A: Number of Subjects With Objective Response (OR) of Complete Response (CR) or Partial Response (PR)

End point title	Cohort 2A: Number of Subjects With Objective Response (OR) of Complete Response (CR) or Partial Response (PR)[2][3]

End point description:

OR was defined as subjects with best overall response (BOR) of CR or PR as assessed by investigator based on response evaluation criteria in solid tumors (RECIST) version (v) 1.1. For OR, the BOR was defined as the best response (CR or PR for >4 weeks) recorded from start of treatment until PD or death whichever occurred first. CR: disappearance of all target and non-target lesions (non-lymph nodes). All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis <10 millimeters (mm). PR: at least a 30% decrease in the sum of diameter (SOD) of target lesions, taking as reference the baseline sum diameters. PD was defined as at least 20% increase (including an absolute

increase of at least 5 mm) in SOD of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. Full analysis set included all enrolled subjects who have not failed study screening.

End point type	Primary

End point timeframe:

From date of first dose of study drug until first documentation of disease progression, or date of death, whichever occurred first (up to approximately 4 years 7 months)

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: No statistical analysis was planned for this endpoint.

[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: No statistical analysis was planned for this endpoint.

End point values	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: subjects	1			

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 2A: Number of Subjects With Best Overall Response (BOR)

End point title	Cohort 2A: Number of Subjects With Best Overall Response (BOR)[4][5]

End point description:

BOR was defined as the best response of CR or PR for >4 weeks or SD for >=7 weeks recorded from the start of the treatment until PD or death, whichever occurred first based on RECIST v1.1. CR: disappearance of all target and non-target lesions (non-lymph nodes). All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis <10 mm. PR: at least a 30% decrease in the SOD of target lesions, taking as reference the baseline sum diameters. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SOD. PD was defined as at least 20% increase (including an absolute increase of at least 5 mm) in the SOD of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. Full analysis set included all enrolled subjects who have not failed study screening.

End point type	Primary

End point timeframe:

From first dose of study drug until disease progression or recurrence of lesions (up to approximately 4 years 7 months)

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: No statistical analysis was planned for this endpoint.

[5] - 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: No statistical analysis was planned for this endpoint.

End point values	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: subjects				
Complete Response	0			
Partial Response	1			
Stable Disease	0			

Statistical analyses

No statistical analyses for this end point

Primary: Cohorts 2B and 3B: Progression-free Survival (PFS) Rate at Month 4

End point title	Cohorts 2B and 3B: Progression-free Survival (PFS) Rate at Month 4[6][7]

End point description:

Progression free survival at Month 4 (PFS-4) rate was defined as the percentage of subjects who were alive and without PD at Month 4 after the first dose of study drug, based on RECIST v1.1, using a binomial proportion with corresponding 95% confidence interval (CI). PD: >= 20% increase in sum of diameters of target lesions, reference-smallest sum recorded in study (sum at baseline if that was smallest). Sum of diameters must have absolute increase of >=5 mm. Appearance of >=1 new lesions also considered PD. Progression free survival at Month 4(PFS-4) evaluable set included all subjects treated with study drug for at least 4 months or those who died or radiologically progressed within 4 months after first dose or received anticancer treatment within 4 months after first dose.

End point type	Primary

End point timeframe:

Month 4

Notes:

[6] - 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: No statistical analysis was planned for this endpoint.

[7] - 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: No statistical analysis was planned for this endpoint.

End point values	Cohort2B,SinglEagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	15		
Units: percentage of subjects				
number (confidence interval 95%)	32.1 (15.9 to 52.4)	66.7 (38.4 to 88.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 3A: Recommended Dose of Lenvatinib When Given in Combination With Etoposide and Ifosfamide

End point title	Cohort 3A: Recommended Dose of Lenvatinib When Given in Combination With Etoposide and Ifosfamide[8]

End point description:

RD:dose that had dose limiting toxicity(DLT)rate closest to 20% rate.DLT:adverse drug reaction and assessed according to common terminology criteria for adverse events(CTCAE)version (v) 4.03 defined as 1) Grade4 neutropenia for more than or equal to(>=)7 days,2) Grade>=3 thrombocytopenia with bleeding,or lasting greater than(>)7 days,3)Grade>=3 febrile neutropenia,4) Next course chemotherapy delayed>=7 days,5) Grade>=3 nonhematologic toxicity persisting >7 days optimal supportive care,6) Grade 4 hypertension,confirmed systolic/diastolic blood pressure>25 millimeters of mercury(mmHg)above 95th percentile for age, or elevated diastolic blood pressure(>95th percentile for age)not controlled by single antihypertensive medication within 14 days use,7) Grade3 proteinuria,8)Any recurrent Grade2 nonhematological toxicity requiring>=2 interruption and dose reductions.Safety analysis set included all subjects who received any study drug and had at least one post-baseline safety evaluation.

End point type	Primary

End point timeframe:

Cycle 1 (21 days)

Notes:

[8] - 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: No statistical analysis was planned for this endpoint.

End point values	Cohort 3A: All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: milligram per meter square (mg/m^2)				
number (not applicable)	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2B, 3A, and 3B: Number of Subjects With Best Overall Response (BOR)

End point title	Cohorts 1, 2B, 3A, and 3B: Number of Subjects With Best Overall Response (BOR)[9]

End point description:

BOR: best response of CR or PR for >4 weeks or SD for >=7 weeks from first dose, recorded from start of treatment until PD or death, whichever occurred first based on RECIST v1.1. CR: disappearance of all target and non-target lesions. All pathological lymph nodes must have reduction in their short axis <10 mm. PR: at least 30% decrease in SOD of target lesions, taking as reference the baseline sum diameters. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SOD. PD: at least 20% increase (including an absolute increase of at least 5 mm) in the SOD of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. Not evaluable means BOR of NE or SD of <7 weeks duration. Full analysis set:all enrolled subjects who have not failed study screening. Number of subjects analysed"=subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug until disease progression or recurrence (up to approximately 4 years 7 months)

Notes:

[9] - 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: No statistical analysis was planned for this endpoint.

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort2B,SinglEagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	10	30
Units: subjects				
Complete Response	0	0	0	0
Partial Response	0	0	0	2
Stable Disease	2	5	4	13
Progressive Disease	1	2	4	12
Not Evaluable	0	2	2	3

End point values	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	14	18	
Units: subjects				
Complete Response	0	0	0	
Partial Response	2	0	3	
Stable Disease	3	10	9	
Progressive Disease	2	2	4	
Not Evaluable	0	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2B, 3A, and 3B: Objective Response Rate (ORR)

End point title	Cohorts 1, 2B, 3A, and 3B: Objective Response Rate (ORR)[10]

End point description:

ORR was defined as the percentage of subjects with a BOR of CR or PR for >4 weeks or SD for >=7 weeks as assessed by investigator based on RECIST v1.1, recorded from start of study treatment until PD or death whichever occurred first. CR was defined as the disappearance of all target and non-target lesions (non-lymph nodes). All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis <10 mm. PR was defined as at least a 30% decrease in the SOD of target lesions, taking as reference the baseline sum diameters. 95% CI of the ORR were calculated according to Clopper and Pearson method. Full analysis set included all enrolled subjects who have not failed study screening. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug to the date of first documentation of disease progression, or date of death, whichever occurred first (up to approximately 4 years 7 months)

Notes:

[10] - 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: No statistical analysis was planned for this endpoint.

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort2B,SinglEagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	10	30
Units: percentage of subjects				
number (confidence interval 95%)	0 (0.0 to 70.8)	0 (0.0 to 33.6)	0 (0.0 to 30.8)	6.7 (0.8 to 22.1)

End point values	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	14	18	
Units: percentage of subjects				
number (confidence interval 95%)	28.6 (3.7 to 71.0)	0 (0.0 to 23.2)	16.7 (3.6 to 41.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Duration of Response (DOR)

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Duration of Response (DOR)

End point description:

DOR was defined as time in months from the first documentation confirmed CR or PR until the first documentation of confirmed PD as assessed by investigator based on RECIST v1.1. CR: disappearance of all target and non-target lesions (non-lymph nodes). All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis <10 mm. PR: at least a 30% decrease in the SOD of target lesions, taking as reference the baseline sum diameters. PD: at least 20% increase (including an absolute increase of at least 5 mm) in the SOD of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. 95% CI for the median were calculated according to Brookmeyer and Crowley method. Full analysis set. Number of subjects analysed=subjects evaluable for endpoint. Here, 99999 and -99999 indicates data could not be estimated as insufficient subjects were available for analysis.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug to first documentation of CR or PR until first documentation of

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	1
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	1.9 (-99999 to 99999)

Notes:

[11] - No subject was analysed for this group.

[12] - No subject was analysed for this group.

[13] - No subject was analysed for this group.

End point values	Cohort2B,SingleagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	0[14]	3
Units: months				
median (confidence interval 95%)	4.6 (-99999 to 99999)	99999 (-99999 to 99999)	(to)	99999 (-99999 to 99999)

Notes:

[14] - No subject was analysed for this group.

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects Who Experienced Disease Control

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects Who Experienced Disease Control

End point description:

Subjects were defined as having disease control if they had a BOR of CR or PR for >4 weeks, or SD (minimum duration from first dose to SD >=7 weeks) or if subjects had a BOR of CR or Non-CR/Non-PD (minimum duration from first dose to Non-CR/Non-PD >=7 weeks) per RECIST v1.1, recorded from first dose until PD or death whichever occurred first. CR: disappearance of all target/non-target lesions (non-lymph nodes). All pathological lymph nodes (target/non-target) must have a reduction in their short axis <10 mm. PR: at least a 30% decrease in the SOD of target lesions, taking as reference the baseline sum diameters. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference smallest SOD. Non-CR/Non-PD: persistence of 1 or more non-target lesions, maintenance of tumor marker level above the normal limits. Full analysis set: all enrolled subjects who have not failed study screening.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug until the date of first documented PD, or date of death, whichever occurred first (up to approximately 4 years and 7 months)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	11	1
Units: subjects	2	5	5	1

End point values	Cohort2B,SinglеagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	7	15	20
Units: subjects	16	5	11	14

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects Experienced Clinical Benefit

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects Experienced Clinical Benefit

End point description:

Subjects were defined as having clinical benefit if they had BOR of CR or PR or durable SD (lasting >=23 weeks) or subjects with evaluable disease who have BOR of CR or durable Non-CR/Non-PD (lasting >=23 weeks) as per RECIST v1.1. BOR: CR or PR for >4 weeks or SD for >5 weeks from first dose,until PD or recurrence based on RECIST v1.1 for target/non-target lesions. CR: disappearance of all target/non-target lesions (non-lymph nodes). All pathological lymph nodes (whether target/non-target) must have reduction in short axis <10 mm. PR: at least 30% decrease in SOD of target lesions, taking reference baseline sum diameters. SD: neither sufficient shrinkage to qualify for PR nor increase to qualify for PD,taking reference smallest SOD.Non-CR/Non-PD:persistence of 1 or more non-target lesions and maintenance of tumor marker level above normal limits.Full analysis set included all enrolled subjects who have not failed study screening.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug until date of first documentation of disease progression, or date of death, whichever occurred first (up to approximately 4 years 7 months)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	11	1
Units: subjects	0	3	4	1

End point values	Cohort2B,SinglеagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	7	15	20
Units: subjects	7	4	5	8

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Progression-free Survival (PFS)

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Progression-free Survival (PFS)

End point description:

PFS was defined as the time (in months) from the date of first dose of study drug to the date of first documentation of disease progression or date of death, whichever occurred first, based on RECIST v1.1. Disease progression was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the baseline sum of diameters of target lesions. 95% CI of median were calculated according to Brookmeyer and Crowley. Full analysis set included all enrolled subjects who have not failed study screening. Here, 99999 and -99999 indicates data could not be estimated as insufficient subjects were available for analysis.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug until date of first documentation of disease progression or date of death, whichever occurred first (up to approximately 4 years 7 months)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	11	1
Units: months				
median (confidence interval 95%)	3.7 (0.5 to 5.0)	6.3 (0.6 to 10.6)	5.5 (1.4 to 11.3)	5.5 (-99999 to 99999)

End point values	Cohort2B,SinglEagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	7	15	20
Units: months				
median (confidence interval 95%)	3.0 (1.8 to 5.4)	7.1 (2.1 to 99999)	12.0 (11.1 to 16.1)	6.9 (4.2 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Time to Progression (TTP)

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Time to Progression (TTP)

End point description:

TTP was defined as the time from the date of first dose of study drug to the date of first documentation of disease progression based on RECIST 1.1. Disease progression was defined as at least a 20% increase (including an absolute increase of at least 5 mm) in the SOD of target lesions, taking as reference the baseline sum of diameters of target lesions. 95% CI of median were calculated according to Brookmeyer and Crowley method. Full analysis set included all enrolled subjects who have not failed study screening. Here, 99999 and -99999 indicates data could not be estimated as insufficient subjects were available for analysis.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug until the date of first documentation of disease progression (up to approximately 4 years 7 months)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	11	1
Units: months				
median (confidence interval 95%)	3.7 (0.5 to 5.0)	6.3 (0.6 to 10.6)	5.5 (1.4 to 11.3)	5.5 (-99999 to 99999)

End point values	Cohort2B,SinglEagentExpansion,	Cohort 3A, Combination Dose-finding:	Cohort 3A, Combination Dose-finding:	Cohort 3B, Combination Expansion:

	Osteosarcoma: Lenvatinib14mg/m^2	Lenvatinib 11 mg/m^2	Lenvatinib 14 mg/m^2	Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	7	15	20
Units: months				
median (confidence interval 95%)	3.0 (1.8 to 5.4)	7.1 (2.1 to 99999)	12.0 (11.1 to 16.1)	6.9 (4.2 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Overall Survival (OS)

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Overall Survival (OS)

End point description:

OS was defined as the time from the date of the first dose of study drug until the date of death from any cause. Subjects who are lost to follow-up and those who are alive at the date of data cutoff were censored at the date the subject was last known to be alive (or the data cutoff date). 95% CI of median were calculated according to Brookmeyer and Crowley method. Full analysis set included all enrolled subjects who have not failed study screening. Here, 99999 indicates data could not be estimated due to low number of subjects with events.

End point type	Secondary

End point timeframe:

From date of the first dose of study drug until the date of death (up to approximately 4 years 7 months)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	11	1
Units: months				
median (confidence interval 95%)	8.1 (3.8 to 99999)	7.4 (1.3 to 99999)	7.7 (2.7 to 99999)	99999 (99999 to 99999)

End point values	Cohort2B,SingleagentExpansion, Osteosarcoma: Lenvatinib14mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	7	15	20
Units: months				
median (confidence interval 95%)	10.0 (5.6 to 12.3)	13.6 (2.4 to 28.0)	99999 (8.8 to 99999)	99999 (7.3 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

Number of subjects with TEAEs (serious and non-serious adverse events) and SAEs were reported based on their safety assessments of hematology, clinical chemistry, urine values, proximal tibial growth, fecal occult blood, physical examinations, regular measurement of vital signs and electrocardiogram parameter values. Safety analysis set included all subjects who received any study drug and had at least one post-baseline safety evaluation.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug up to 30 days after the last dose (up to approximately 7 years)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	11	7	1
Units: subjects				
TEAEs	5	11	7	1
SAEs	3	7	5	1

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	11	11	20
Units: subjects				
TEAEs	29	11	11	20
SAEs	21	7	9	16

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A, and 3B: Number of Subjects With Shift From Baseline to Worst Post Baseline Measurements on Urine DipStick for Proteinuria

End point title	Cohorts 1, 2A, 2B, 3A, and 3B: Number of Subjects With Shift From Baseline to Worst Post Baseline Measurements on Urine DipStick for Proteinuria

End point description:

An aliquot of the urine samples were collected to analyze protein by dipstick method, microscopic examination (if protein is abnormal). The dipstick test gives results in a semi-quantitative manner and results for urinalysis parameters of urine protein can be read as “negative, Trace, plus (+) 1, +2, +3 and +4” indicating proportional concentrations in the urine sample. The plus sign increases with a higher level of proteins in the urine. Safety analysis set included all subjects who received any study drug and had at least one post-baseline safety evaluation. Here "number of subjects analysed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to approximately 4 years 7 months

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	11	7	1
Units: subjects				
Baseline: Trace, Worst Post baseline: Negative	2	2	0	0
Baseline: Trace, Worst Post baseline: Trace	1	0	0	0
Baseline: +1, Worst Post baseline: Negative	2	3	1	0
Baseline: +1, Worst Post baseline: +1	0	0	1	0
Baseline: Negative, Worst Post baseline: Negative	0	1	0	1
Baseline: +2, Worst Post baseline: Negative	0	2	1	0
Baseline: +3, Worst Post baseline: Negative	0	1	1	0
Baseline: +3, Worst Post baseline: +1	0	1	0	0
Baseline: +3, Worst Post baseline: +2	0	1	0	0
Baseline: +3, Worst Post baseline: Trace	0	0	1	0
Baseline: +4, Worst Post baseline: Trace	0	0	1	0

Baseline: +4, Worst Post baseline: +1	0	0	1	0
Baseline: Negative, Worst Post baseline: Trace	0	0	0	0
Baseline: Negative, Worst Post baseline: +1	0	0	0	0
Baseline: Negative, Worst Post baseline: +2	0	0	0	0
Baseline: Negative, Worst Post baseline: +3	0	0	0	0
Baseline: Trace, Worst Post baseline: +1	0	0	0	0
Baseline: Trace, Worst Post baseline: +2	0	0	0	0
Baseline: Trace, Worst Post baseline: +3	0	0	0	0
Baseline: +1, Worst Post baseline: Trace	0	0	0	0
Baseline: +1, Worst Post baseline: +2	0	0	0	0
Baseline: +1, Worst Post baseline: +3	0	0	0	0
Baseline: Negative, Worst Post baseline: +4	0	0	0	0
Baseline: +1, Worst Post baseline: +4	0	0	0	0

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	11	11	20
Units: subjects				
Baseline: Trace, Worst Post baseline: Negative	0	0	0	0
Baseline: Trace, Worst Post baseline: Trace	1	0	1	1
Baseline: +1, Worst Post baseline: Negative	0	0	0	0
Baseline: +1, Worst Post baseline: +1	0	0	0	0
Baseline: Negative, Worst Post baseline: Negative	4	0	4	2
Baseline: +2, Worst Post baseline: Negative	1	0	0	0
Baseline: +3, Worst Post baseline: Negative	0	0	0	0
Baseline: +3, Worst Post baseline: +1	0	0	0	0
Baseline: +3, Worst Post baseline: +2	0	0	0	0
Baseline: +3, Worst Post baseline: Trace	0	0	0	0
Baseline: +4, Worst Post baseline: Trace	0	0	0	0
Baseline: +4, Worst Post baseline: +1	1	0	0	0
Baseline: Negative, Worst Post baseline: Trace	5	0	1	3
Baseline: Negative, Worst Post baseline: +1	7	7	1	1

Baseline: Negative, Worst Post baseline: +2	1	1	1	6
Baseline: Negative, Worst Post baseline: +3	1	1	2	2
Baseline: Trace, Worst Post baseline: +1	2	1	0	0
Baseline: Trace, Worst Post baseline: +2	1	0	0	1
Baseline: Trace, Worst Post baseline: +3	1	0	0	1
Baseline: +1, Worst Post baseline: Trace	1	0	0	0
Baseline: +1, Worst Post baseline: +2	3	0	0	1
Baseline: +1, Worst Post baseline: +3	1	1	0	0
Baseline: Negative, Worst Post baseline: +4	0	0	1	1
Baseline: +1, Worst Post baseline: +4	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Shift From Baseline to Worst Post Baseline Score in Lansky Performance Play Score

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Shift From Baseline to Worst Post Baseline Score in Lansky Performance Play Score

End point description:

Lansky Performance Play Scale:rates a child’s activity level for <16 years of age.Scores on scale range from 0(unresponsive)to 100(fully active, normal),where 100=fully active,normal;90=minor restrictions in physically strenuous activity;80=active,but tires more quickly;70=both greater restriction of and less time spent in play activity;60=up and around, but minimal active play,keeps busy with quieter activities;50=gets dressed,but lies around much of day,no active play,able to subject in quiet play and activities;40=mostly in bed,participates in quiet activities;30=in bed,needs assistance even for quiet play;20=often sleeping,play entirely limited to very passive activities;10=no play,does not get out of bed;0=unresponsive.Higher score indicates more activity and lower indicates less or no activity.Safety analysis set:all subjects who received drug and had at least 1 postbaseline safety evaluation. Number of subjects analysed=subjects evaluable for endpoint.

End point type	Secondary

End point timeframe:

Baseline up to approximately 4 years 7 months

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	7	7	1
Units: subjects				
Baseline score:100%, Worst Postbaseline score:90%	3	0	0	0

Baseline score: 70%, Worst Postbaseline score: 60%	0	1	0	0
Baseline score: 80%, Worst Postbaseline score: 60%	0	1	1	0
Baseline score: 100%, Worst Postbaseline score:60%	0	1	0	0
Baseline score: 80%, Worst Postbaseline score: 70%	0	1	0	0
Baseline score: 90%, Worst Postbaseline score: 70%	0	1	0	0
Baseline score: 90%, Worst Postbaseline score: 80%	0	1	1	0
Baseline score:100%, Worst Postbaseline score:100%	0	1	0	1
Baseline score: 80%, Worst Postbaseline score: 40%	0	0	1	0
Baseline score: 70%, Worst Postbaseline score: 80%	0	0	1	0
Baseline score: 80%, Worst Postbaseline score: 80%	0	0	1	0
Baseline score: 100%, Worst Postbaseline score:80%	0	0	1	0
Baseline score: 90%, Worst Postbaseline score: 90%	0	0	1	0
Baseline score: 60%, Worst Postbaseline score: 60%	0	0	0	0
Baseline score: 90%, Worst Postbaseline score: 60%	0	0	0	0
Baseline score: 70%, Worst Postbaseline score: 70%	0	0	0	0
Baseline score: 90%, Worst Postbaseline score:100%	0	0	0	0
Baseline score: 100%, Worst Postbaseline score:70%	0	0	0	0
Baseline score: 80%, Worst Postbaseline score: 50%	0	0	0	0

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	6	7	9
Units: subjects				
Baseline score:100%, Worst Postbaseline score:90%	1	1	1	0
Baseline score: 70%, Worst Postbaseline score: 60%	0	0	0	0
Baseline score: 80%, Worst Postbaseline score: 60%	1	1	0	0
Baseline score: 100%, Worst Postbaseline score:60%	0	0	0	0
Baseline score: 80%, Worst Postbaseline score: 70%	0	0	3	0
Baseline score: 90%, Worst Postbaseline score: 70%	1	0	0	0

Baseline score: 90%, Worst Postbaseline score: 80%	1	0	0	0
Baseline score:100%, Worst Postbaseline score:100%	0	0	0	5
Baseline score: 80%, Worst Postbaseline score: 40%	0	0	0	0
Baseline score: 70%, Worst Postbaseline score: 80%	0	0	1	0
Baseline score: 80%, Worst Postbaseline score: 80%	2	2	0	2
Baseline score: 100%, Worst Postbaseline score:80%	0	1	0	0
Baseline score: 90%, Worst Postbaseline score: 90%	4	0	1	2
Baseline score: 60%, Worst Postbaseline score: 60%	1	0	0	0
Baseline score: 90%, Worst Postbaseline score: 60%	1	0	0	0
Baseline score: 70%, Worst Postbaseline score: 70%	1	0	1	0
Baseline score: 90%, Worst Postbaseline score:100%	1	0	0	0
Baseline score: 100%, Worst Postbaseline score:70%	0	1	0	0
Baseline score: 80%, Worst Postbaseline score: 50%	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Shift From Baseline to Worst Post Baseline Score in Karnofsky Performance Status (KPS) Scores

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Shift From Baseline to Worst Post Baseline Score in Karnofsky Performance Status (KPS) Scores

End point description:

KPS:compare effectiveness of medicine for disease and assess outcomes in subjects. KPS Scores:recorded on 11point scale(0,10, 20,30,40,50,60,70,80,90 and 100%),where 0=Dead;10=moribund,fatal processes progressing rapidly;20=very sick,hospital admission necessary,active supportive treatment necessary;30=severely disabled,hospital admission is indicated although death not imminent;40=disabled,requires special care/assistance;50=requires considerable assistance/frequent medical care;60=requires occasional assistance,but is able to care for personal needs;70=cares for self,unable to carry normal activity or active work;80=normal activity with effort,some signs of disease; 90=able to carry on normal activity,minor signs of disease;100=normal no complaints,no evidence of disease.Lower score,worse survival for most serious illnesses.Safety Analysis Set:all subjects who received drug,had at least 1 postbaseline safety evaluation.Number of subjects

End point type	Secondary

End point timeframe:

Baseline up to approximately 4 years 7 months

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	1	0[15]	1
Units: subjects				
Baseline score: 100%, Worst Postbaseline score:80%	1	0		0
Baseline score: 100%, Worst Postbaseline score:90%	0	1		0
Baseline score: 70%, Worst Postbaseline score: 70%	0	0		0
Baseline score: 90%, Worst Postbaseline score: 70%	0	0		0
Baseline score: 80%, Worst Postbaseline score: 80%	0	0		0
Baseline score: 90%, Worst Postbaseline score: 60%	0	0		0
Baseline score:100%, Worst Postbaseline score:100%	0	0		1
Baseline score: 100%, Worst Postbaseline score:70%	0	0		0
Baseline score: 90%, Worst Postbaseline score: 80%	0	0		0
Baseline score: 90%, Worst Postbaseline score: 90%	0	0		0

Notes:

[15] - Here "number of subjects analysed" signifies subjects who were analysed for this endpoint.

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	3	1	9
Units: subjects				
Baseline score: 100%, Worst Postbaseline score:80%	2	0	0	2
Baseline score: 100%, Worst Postbaseline score:90%	2	1	0	2
Baseline score: 70%, Worst Postbaseline score: 70%	1	0	1	0
Baseline score: 90%, Worst Postbaseline score: 70%	1	0	0	0
Baseline score: 80%, Worst Postbaseline score: 80%	1	0	0	0
Baseline score: 90%, Worst Postbaseline score: 60%	0	1	0	0
Baseline score:100%, Worst Postbaseline score:100%	1	1	0	1
Baseline score: 100%, Worst Postbaseline score:70%	0	0	0	2
Baseline score: 90%, Worst Postbaseline score: 80%	1	0	0	1

Baseline score: 90%, Worst Postbaseline score: 90%	3	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Most Frequent Treatment-emergent Adverse Events Related to Lenvatinib Exposure

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Most Frequent Treatment-emergent Adverse Events Related to Lenvatinib Exposure

End point description:

Safety analysis set included all subjects who received any study drug and had at least one post-baseline safety evaluation.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug up to 30 days after the last dose of study drug (up to approximately 4 years 7 months)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	11	7	1
Units: subjects				
Hypothyroidism	3	6	3	0
Abdominal pain	2	2	1	1
Diarrhea	3	5	3	1
Nausea	1	2	3	0
Vomiting	1	6	3	0
Asthenia	2	1	0	0
Fatigue	0	2	3	0
Alanine aminotransferase increased increased	0	2	1	0
Blood thyroid stimulating hormone increased	3	0	0	0
Weight decreased	3	4	1	0
Decreased appetite	0	5	1	0
Arthralgia	1	2	1	0
Myalgia	0	2	0	0
Pain in extremity	0	2	1	0
Headache	0	1	1	0
Proteinuria	0	3	3	0
Dysphonia	1	0	0	0
Erythema	1	1	1	0

Hair color changes	2	1	1	0
Palmar-plantar erythrodysaesthesia	0	2	0	0
Hypertension	0	3	4	1
Haematuria	0	0	0	0
Hypokalaemia	0	0	0	0
Hypophosphataemia	0	0	0	0
Platelet count decreased	0	0	0	0
Back pain	0	0	0	0
Dry skin	0	0	0	0
Oral pain	0	0	0	0
Pneumothorax	0	0	0	0
Dehydration	0	0	0	0
Hypoalbuminaemia	0	0	0	0
Lethargy	0	0	0	0
Leukopenia	0	0	0	0
Neutrophil count decreased	0	0	0	0
Oral dysaesthesia	0	0	0	0
Oropharyngeal pain	0	0	0	0
Proctalgia	0	0	0	0
Toxic encephalopathy	0	0	0	0
Lymphocyte count decreased	0	0	0	0
Abdominal pain upper	0	0	0	0
Hyperuricemia	0	0	0	1
Insomnia	0	0	0	1
Anaemia	0	0	0	0
Neutropenia	0	0	0	0
Epistaxis	0	0	0	0
Thrombocytopenia	0	0	0	0
Febrile neutropenia	0	0	0	0
Stomatitis	0	0	0	0
Constipation	0	0	0	0
White blood cell count decreased	0	0	0	0
Lymphopenia	0	0	0	0
Haematochezia	0	0	0	0
Pyrexia	0	0	0	0
Wound dehiscence	0	0	0	0
Hypocalcaemia	0	0	0	0
Dizziness	0	0	0	0
Dyspnoea	0	0	0	0
Hyperhidrosis	0	0	0	0

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	11	11	20
Units: subjects				

Hypothyroidism	13	5	6	6
Abdominal pain	5	6	5	6
Diarrhea	8	5	5	12
Nausea	8	7	8	13
Vomiting	7	5	6	12
Asthenia	8	0	0	7
Fatigue	8	2	4	3
Alanine aminotransferase increased increased	1	3	1	4
Blood thyroid stimulating hormone increased	9	3	0	5
Weight decreased	6	5	3	4
Decreased appetite	13	4	2	5
Arthralgia	1	2	4	1
Myalgia	1	0	0	0
Pain in extremity	0	3	1	0
Headache	5	2	4	4
Proteinuria	7	2	5	8
Dysphonia	5	0	0	0
Erythema	0	0	0	0
Hair color changes	2	0	0	0
Palmar-plantar erythrodysaesthesia	1	1	2	0
Hypertension	10	1	4	3
Haematuria	0	4	1	4
Hypokalaemia	0	4	1	2
Hypophosphataemia	0	3	2	2
Platelet count decreased	0	2	3	11
Back pain	0	2	2	2
Dry skin	0	2	2	0
Oral pain	0	2	2	1
Pneumothorax	0	2	2	1
Dehydration	0	2	1	4
Hypoalbuminaemia	0	2	1	0
Lethargy	0	2	1	2
Leukopenia	0	1	2	3
Neutrophil count decreased	0	2	1	9
Oral dysaesthesia	0	2	1	0
Oropharyngeal pain	0	1	2	1
Proctalgia	0	2	1	0
Toxic encephalopathy	0	1	2	0
Lymphocyte count decreased	0	2	0	4
Abdominal pain upper	0	1	0	4
Hyperuricemia	0	0	0	0
Insomnia	0	0	0	0
Anaemia	0	9	7	15
Neutropenia	0	6	6	8
Epistaxis	0	5	4	4
Thrombocytopenia	0	5	4	5
Febrile neutropenia	0	5	3	2
Stomatitis	0	4	4	4
Constipation	0	5	2	2
White blood cell count decreased	0	4	3	12

Lymphopenia	0	2	0	0
Haematochezia	0	0	2	0
Pyrexia	0	2	0	0
Wound dehiscence	0	0	2	0
Hypocalcaemia	0	2	0	0
Dizziness	0	0	2	0
Dyspnoea	0	2	0	0
Hyperhidrosis	0	0	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A, and 3B: Plasma Concentrations of Lenvatinib

End point title	Cohorts 1, 2A, 2B, 3A, and 3B: Plasma Concentrations of Lenvatinib

End point description:

Duration of each cycle for Cohorts 1, 2A, 2B is 28 days. Duration of each cycle for Cohorts 3A, 3B is 21 days. Pharmacokinetic (PK) Analysis Set included all subjects who had received any study drug and had evaluable PK data. Here "subjects analysed" signifies subjects who were evaluable for this endpoint at given time points. Here, 99999 indicates standard deviation could not be calculated because only one subject was available for analysis.

End point type	Secondary

End point timeframe:

Cohorts 1, 2A, 2B: Cycle(C)1 Day(D)1: 0.5-4 hours (h), 6-10 h post-dose, C1D15: pre-dose, 0.5-4 h, 6-10 h post-dose, C2D1: pre-dose, 2-12 h post-dose; Cohorts 3A, 3B: C1D1: 0.5-4 h, 6-10 h post-dose, C2D1: pre-dose, 2-12 h post-dose

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	11	7	1
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1: 0.5-4 hours(n=5,11,7,1,29,11,11,20)	295.6 (± 214.01)	134.8 (± 145.83)	52.5 (± 81.40)	11.1 (± 99999)
Cycle 1 Day 1: 6-10 hours(n=5,11,7,1,30,11,11,20)	212.7 (± 185.98)	281.9 (± 137.39)	238.0 (± 135.87)	188 (± 99999)
Cycle 1 Day 15: Pre-dose(n=4,9,6,1,29,0,0,0)	46.9 (± 11.01)	59.1 (± 29.19)	96.9 (± 66.10)	56.2 (± 99999)
Cycle 1 Day 15: 0.5-4 hours(n=4,8,6,1,28,0,0,0)	133.4 (± 163.37)	226.6 (± 204.61)	191.8 (± 190.22)	124 (± 99999)
Cycle 1 Day 15: 6-10 hours(n=4,8,6,1,29,0,0,0)	351.8 (± 157.15)	375.8 (± 121.21)	413.0 (± 221.47)	247 (± 99999)
Cycle 2 Day 1: Pre-dose(n=5,8,7,1,27,11,8,17)	58.1 (± 19.58)	61.6 (± 60.61)	97.9 (± 77.08)	59.8 (± 99999)
Cycle 2 Day 1: 2-12 hours(n=5,7,7,1,28,11,9,18)	502.4 (± 360.71)	440.7 (± 229.29)	339.2 (± 212.44)	102 (± 99999)

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	11	11	20
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1: 0.5-4 hours(n=5,11,7,1,29,11,11,20)	177.4 (± 191.03)	105.2 (± 131.54)	111.4 (± 131.47)	209.7 (± 197.66)
Cycle 1 Day 1: 6-10 hours(n=5,11,7,1,30,11,11,20)	289.4 (± 200.09)	191.9 (± 100.69)	148.5 (± 122.41)	164.8 (± 73.59)
Cycle 1 Day 15: Pre-dose(n=4,9,6,1,29,0,0,0)	67.0 (± 53.78)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 1 Day 15: 0.5-4 hours(n=4,8,6,1,28,0,0,0)	168.3 (± 157.67)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 1 Day 15: 6-10 hours(n=4,8,6,1,29,0,0,0)	322.9 (± 138.87)	0 (± 0)	0 (± 0)	0 (± 0)
Cycle 2 Day 1: Pre-dose(n=5,8,7,1,27,11,8,17)	66.8 (± 62.50)	51.7 (± 44.23)	76.1 (± 63.25)	50.4 (± 65.10)
Cycle 2 Day 1: 2-12 hours(n=5,7,7,1,28,11,9,18)	382.4 (± 217.49)	205.6 (± 134.66)	237.4 (± 124.82)	275.3 (± 135.73)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2B, 3B: Percent Change From Baseline in Serum Biomarkers Level

End point title	Cohort 2B, 3B: Percent Change From Baseline in Serum Biomarkers Level

End point description:

Serum biomarkers included Fibroblast Growth Factor (FGF) 19, FGF 21, Vascular Endothelial Growth Factor (VEGF). In this outcome measure, percent change from baseline in serum biomarkers level per "PFS-4, Yes" and "PFS-4, No" have been reported. As per assessment of investigator based on RECIST v1.1, "PFS-4, Yes"= subjects evaluable for PFS-4 month and alive and without PD at 4 months from the first dose, "PFS-4, No"=subjects evaluable for PFS-4 month and not alive or with PD at 4 months from the first dose. PFS-4 evaluable set: all subjects treated with study drug for at least 4 months or those who died or radiologically progressed within 4 months after first dose or received anticancer treatment within 4 months after first dose. Here "number of subjects analysed" signifies subjects who were evaluable for this endpoint. "n" signifies subjects who were evaluable for this endpoint for specified categories.

End point type	Secondary

End point timeframe:

Cohort 2B: Baseline, Cycle 2-3 Day 1 (Duration of each cycle=28 days); Cohort 3B: Baseline, Cycle 2 Day 1, Cycle 4 Day 1

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	9		
Units: percent change				
arithmetic mean (standard deviation)				
C2D1: FGF 19 (PFS-4, Yes) (n=8, 9)	48.7 (± 110.78)	172.1 (± 211.86)		
C2D1: FGF 19 (PFS-4, No) (n=18, 4)	109.9 (± 139.19)	78.3 (± 203.30)		
C3D1: FGF 19 (PFS-4, Yes) (n=9, 0)	47.3 (± 130.42)	0 (± 0)		
C3D1: FGF 19 (PFS-4, No) (n=8, 0)	194.5 (± 180.71)	0 (± 0)		
C4D1: FGF 19 (PFS-4, Yes) (n=0, 9)	0 (± 0)	237.7 (± 204.94)		
C4D1: FGF 19 (PFS-4, No) (n=0, 1)	0 (± 0)	91.9 (± 99999)		
C2D1: FGF 21 (PFS-4, Yes) (n=8, 9)	-14.9 (± 68.95)	70.2 (± 138.90)		
C2D1: FGF 21 (PFS-4, No) (n=18, 4)	134.3 (± 203.81)	7.2 (± 48.64)		
C3D1: FGF 21 (PFS-4, Yes) (n=9, 0)	55.0 (± 125.51)	0 (± 0)		
C3D1: FGF 21 (PFS-4, No) (n=8, 0)	17.0 (± 88.92)	0 (± 0)		
C4D1: FGF 21 (PFS-4, Yes) (n=0, 9)	0 (± 0)	256.2 (± 323.34)		
C4D1: FGF 21 (PFS-4, No) (n=0, 1)	0 (± 0)	-1.5 (± 99999)		
C2D1: VEGF (PFS-4, Yes) (n=7, 9)	119.9 (± 309.01)	87.9 (± 105.60)		
C2D1: VEGF (PFS-4, No) (n=18, 4)	124.2 (± 212.18)	95.8 (± 92.53)		
C3D1: VEGF (PFS-4, Yes) (n=8, 0)	64.3 (± 153.50)	0 (± 0)		
C3D1: VEGF (PFS-4, No) (n=8, 0)	23.2 (± 69.67)	0 (± 0)		
C4D1: VEGF (PFS-4, Yes) (n=0, 9)	0 (± 0)	84.3 (± 97.85)		
C4D1: VEGF (PFS-4, No) (n=0, 0)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Overall Palatability and Acceptability Questionnaire Score for Suspension of Lenvatinib

End point title	Cohorts 1, 2A, 2B, 3A and 3B: Number of Subjects With Overall Palatability and Acceptability Questionnaire Score for Suspension of Lenvatinib

End point description:

The palatability and acceptability was assessed using a questionnaire for suspension of lenvatinib questionnaire based on following domains: taste, appearance, smell, how does it feel in the mouth and overall acceptability. Overall palatability and acceptability was assessed on a 7-point Hedonic scale which is a Visual Analog Scale (VAS) graded as follows: 1=super bad, 2=really bad, 3=bad, 4=may be good or may be bad, 5=good, 6=really good, 7=super good. In this measure, number of subjects per

grading for overall palatability and acceptability has been reported. Palatability analysis set included all subjects who received oral suspension of lenvatinib and answered at least 1 question in the palatability questionnaire case report form.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Cycle length=28 days for Cohorts 1, 2A, 2B; Cycle length=21 days for Cohorts 3A, 3B)

End point values	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[16]	2	1	0[17]
Units: subjects				
Good		1	0	
May be Good or May be Bad		0	0	
Bad		0	0	
Really Bad		1	0	
Super Bad		0	1	

Notes:

[16] - Here "subject analysed" signifies subjects who were evaluable for this endpoint.

[17] - Here "subject analysed" signifies subjects who were evaluable for this endpoint.

End point values	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	0[18]	1	4
Units: subjects				
Good	1		1	1
May be Good or May be Bad	0		0	1
Bad	0		0	1
Really Bad	0		0	1
Super Bad	0		0	0

Notes:

[18] - Here "subject analysed" signifies subjects who were evaluable for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of study drug up to 30 days after the last dose (up to approximately 7 years)

Adverse event reporting additional description:

Safety analysis set included all subjects who received any study drug and had at least one post-baseline safety evaluation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2

Reporting group description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 11 mg/m^2 (administered perbody surface area[BSA]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallowcapsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity,subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or studytermination by the sponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2lenvatinib before receiving lenvatinib 11 mg/m^2 in Cycle 1 in Cohort 1. Duration of each treatment cycle in Cohort1=28 days. After determining RD in Cohort1, subjects were enrolled in Cohorts 2A,2B and 3A.

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects (of age group 2 to <6 years and 6 to <18 years) with relapsed or refractory solid malignant tumors received lenvatinib 14 mg/m^2 (administered perBSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given assuspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliancewith safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by subject at any time, or study termination by thesponsor, whichever occurred first. Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib beforereceiving lenvatinib 14 mg/m^2 in Cycle 1 in Cohort 1. Duration of each cycle in Cohort 1=28 days. After determining RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Lenvatinib 5 mg /m^2

Reporting group description:

Eligible subjects of age group 2 to <6 years first underwent a 21-day run-in period with 5 mg/m^2 lenvatinib before receiving lenvatinib 11 mg/m^2 or 14 mg/m^2 in Cohort 1 (Single-agent Dose-finding) Cycle 1.

Reporting group title	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2

Reporting group description:

Subjects (of age group 6 to <18 years) with relapsed or refractory solid malignant tumors received dose of lenvatinib 17 mg/m^2 (administered per BSA) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension),orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity, subject noncompliance with safety orefficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whichever occurred first. Duration of each cycle in Cohort 1=28 days. After determining the RD in Cohort 1, subjects were enrolled in Cohorts 2A, 2B and 3A.

Reporting group title	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib14mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24 mg/day) as capsule orsuspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally, oncedaily on Days 1 to 28 of each treatment cycle as a single agent until disease progression,

intolerable toxicity, subject noncompliance with safety or efficacyassessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, or study termination by the sponsor, whicheveroccurred first. Duration of each treatment cycle in Cohort 2B=28 days.

Reporting group title	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with 131 iodine-refractory differentiated thyroid cancer (DTC) received lenvatinib 14 mg/m^2 (administered per BSA with daily dose capped at 24milligram per day [mg/day]) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallowcapsules and given as suspension), orally, once daily on Days 1 to 28 of each treatment cycle as a single agent until disease progression, intolerable toxicity,subject noncompliance with safety or efficacy assessments, initiation of another anticancer therapy, voluntary discontinuation by the subject at any time, orstudy termination by the sponsor, whichever occurred first. Duration of each cycle=28 days.

Reporting group title	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsulesor suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally,once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/dayintravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3B=21 days.

Reporting group title	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 14 mg/m^2 (administrated per BSA with daily dose capped at 24 mg/day) as capsulesor suspension (lenvatinib capsules were dissolved in water or apple juice for subjects who were unable to swallow capsules and given as suspension), orally,once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000 mg/m^2/day intravenously and etoposide 100 mg/m^2/dayintravenously on Days 1 to 3 of each treatment cycle for up to a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Reporting group title	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2

Reporting group description:

Subjects with relapsed or refractory osteosarcoma received lenvatinib 11 mg/m^2 (20 percent [%] lower than the recommended dose from Cohort 1;administered per BSA with daily dose capped at 24 mg/day) as capsules or suspension (lenvatinib capsules were dissolved in water or apple juice for subjectswho were unable to swallow capsules and given as suspension), orally, once daily on Days 1 to 21 of each treatment cycle in combination with ifosfamide 3000milligram per square meter per day (mg/m^2/day) intravenously and etoposide 100 mg/m^2/day intravenously on Days 1 to 3 of each treatment cycle for upto a total of 5 cycles as a combination therapy. Duration of each treatment cycle in Cohort 3A=21 days. After determining the RD in Cohort 3A, subjects were enrolled in Cohort 3B.

Serious adverse events	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Lenvatinib 5 mg /m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	7 / 11 (63.64%)	0 / 2 (0.00%)
number of deaths (all causes)	1	3	0
number of deaths resulting from adverse events	1	3	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			

subjects affected / exposed	0 / 5 (0.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Malignant neoplasm progression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Lymphoedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Venoocclusive disease			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Gait disturbance			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
General physical health deterioration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Facial pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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, thoracic and mediastinal disorders			

Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 distress			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (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
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (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
Respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Pleuritic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			

Suicide attempt			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
White blood cell count decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Post procedural haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Wound dehiscence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Accidental overdose			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Allergic transfusion reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 pseudoaneurysm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Cardiac arrest			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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

Sinus bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Depressed level of consciousness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Spinal cord compression			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Ischaemic stroke			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Brain injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Dysmetria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Anaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Lymphopenia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Pancytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Colitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Enterocolitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (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
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Gingival bleeding			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Intestinal obstruction			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Anal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Pancreatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Renal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 failure			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Intervertebral disc compression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Pathological fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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			
Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (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
Wound infection bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Vulvitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Transfusion related complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (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	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib 14mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)	21 / 31 (67.74%)	1 / 1 (100.00%)
number of deaths (all causes)	1	4	0
number of deaths resulting from adverse events	1	4	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Myelodysplastic syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Arterial thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Lymphoedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Venoocclusive disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (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
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (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
Respiratory distress			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumothorax			
subjects affected / exposed	0 / 7 (0.00%)	4 / 31 (12.90%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Pleuritic pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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			
Suicide attempt			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 pressure increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (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

Ejection fraction decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (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
Lipase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Platelet count decreased			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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			
Post procedural haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Wound dehiscence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Accidental overdose			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Allergic transfusion reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 pseudoaneurysm			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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			
Cardiac arrest			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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			

Depressed level of consciousness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Spinal cord compression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Ischaemic stroke			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Brain injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Dysmetria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (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	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Febrile neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Leukopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Pancytopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Enterocolitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Stomatitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Anal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Pancreatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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			
Renal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Renal failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back pain			
subjects affected / exposed	0 / 7 (0.00%)	4 / 31 (12.90%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	2 / 7 (28.57%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc compression			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Pathological fracture			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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			
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Bacteraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Influenza			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Wound infection bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Vulvitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Transfusion related complication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (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
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (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	Cohort 3B,	Cohort 3A,	Cohort 3A,

	Combination Expansion: Lenvatinib 14 mg/m^2	Combination Dose-finding: Lenvatinib 14 mg/m^2	Combination Dose-finding: Lenvatinib 11 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 20 (80.00%)	9 / 11 (81.82%)	7 / 11 (63.64%)
number of deaths (all causes)	2	0	2
number of deaths resulting from adverse events	2	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Myelodysplastic syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Arterial thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Lymphoedema			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Venoocclusive disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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			
Gait disturbance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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	2 / 20 (10.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial pain			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Influenza like illness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pneumothorax			
subjects affected / exposed	3 / 20 (15.00%)	2 / 11 (18.18%)	2 / 11 (18.18%)
occurrences causally related to treatment / all	4 / 4	2 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			

subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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 pressure increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Ejection fraction decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Lipase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Platelet count decreased			
subjects affected / exposed	4 / 20 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	12 / 12	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Neutrophil count decreased			
subjects affected / exposed	4 / 20 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	18 / 18	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	5 / 20 (25.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	16 / 16	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Wound dehiscence			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Accidental overdose			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Allergic transfusion reaction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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 pseudoaneurysm			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Cardiac disorders			

Cardiac arrest			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Sinus bradycardia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Bradycardia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Cardiac failure			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Spinal cord compression			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Brain injury			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Toxic encephalopathy			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (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
Headache			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Dysmetria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	5 / 5	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	2 / 20 (10.00%)	3 / 11 (27.27%)	5 / 11 (45.45%)
occurrences causally related to treatment / all	5 / 5	4 / 4	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (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
Thrombocytopenia			

subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Pancytopenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Enterocolitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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	2 / 20 (10.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	4 / 4	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival bleeding			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Intestinal obstruction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Gastritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal inflammation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Pancreatitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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 failure			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Urinary retention			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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			
Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (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
Intervertebral disc compression			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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

Pathological fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (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			
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (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
Influenza			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (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
Wound infection bacterial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulvitis			

subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Transfusion related complication			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1, Single-agent Dose-finding: Lenvatinib 11 mg/m^2	Cohort 1, Single-agent Dose-finding: Lenvatinib 14 mg/m^2	Lenvatinib 5 mg /m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	11 / 11 (100.00%)	2 / 2 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 5 (40.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	2	2	0
Malignant pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Pericardial effusion malignant			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Tumour pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	2 / 5 (40.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences (all)	2	3	0
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Superior vena cava syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	2 / 5 (40.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	4	1	0
Axillary pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Catheter site bruise			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Catheter site dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Catheter site swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Device related thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 5 (40.00%)	3 / 11 (27.27%)	1 / 2 (50.00%)
occurrences (all)	4	4	1
Inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion site irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	6	0	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	5	0
Pyrexia			
subjects affected / exposed	2 / 5 (40.00%)	4 / 11 (36.36%)	1 / 2 (50.00%)
occurrences (all)	8	9	1
Swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Injection site mass			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sensation of foreign body			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			

Balanoposthitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Genital pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Amenorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Genital lesion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Perineal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Premature menopause			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 5 (40.00%)	3 / 11 (27.27%)	1 / 2 (50.00%)
occurrences (all)	3	3	1
Dysaesthesia pharynx			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dysphonia			

subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Dyspnoea			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	2 / 5 (40.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences (all)	3	3	0
Hypoxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pharyngeal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	6	0	0
Productive cough			

subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Respiratory distress			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	2 / 5 (40.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	2 / 5 (40.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Depression			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Nightmare			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Major depression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	4 / 11 (36.36%)	0 / 2 (0.00%)
occurrences (all)	0	6	0
Amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Blood calcium decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood uric acid decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Culture stool positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Full blood count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lipase decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Thyroglobulin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Thyroxine decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	3 / 5 (60.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences (all)	13	6	0
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Occult blood positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Thyroxine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Allergic transfusion reaction			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Wound dehiscence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Anaemia postoperative			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ankle fracture			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Post procedural complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			

subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	5	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Left ventricular dysfunction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Sinus bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ventricular dysfunction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiac dysfunction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiotoxicity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Bundle branch block right			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Systolic dysfunction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amputation stump pain			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cranial nerve paralysis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dysaesthesia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 5 (20.00%)	6 / 11 (54.55%)	0 / 2 (0.00%)
occurrences (all)	2	9	0
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Monoparesis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Muscle contractions involuntary			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Phantom pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pyramidal tract syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Sensory disturbance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Toxic encephalopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Acquired antithrombin III deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Anaemia			
subjects affected / exposed	1 / 5 (20.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	2	2	0
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Polycythaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye discharge			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye ulcer			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Papilloedema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	2 / 5 (40.00%)	7 / 11 (63.64%)	1 / 2 (50.00%)
occurrences (all)	3	9	1
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Anal fistula			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Anal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Anal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Anal pruritus			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Anal skin tags			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 5 (20.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	1	2	0
Diarrhoea			
subjects affected / exposed	4 / 5 (80.00%)	5 / 11 (45.45%)	1 / 2 (50.00%)
occurrences (all)	5	9	1
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dyschezia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Dyspepsia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Eructation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Glossitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0

Nausea			
subjects affected / exposed	3 / 5 (60.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	8	4	0
Noninfective gingivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Oesophageal obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oral discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oral dysaesthesia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	2	6	0
Oral pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pancreatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Perianal erythema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Proctalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Proctitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Stomatitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)	7 / 11 (63.64%)	0 / 2 (0.00%)
occurrences (all)	9	20	0
Anal fissure haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Alopecia			

subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dermatitis bullous			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	1 / 2 (50.00%)
occurrences (all)	1	1	1
Eczema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	1 / 2 (50.00%)
occurrences (all)	1	1	1
Hair colour changes			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hyperkeratosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Onychalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pain of skin			

subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 5 (40.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	4	2	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	0	4	0
Rash			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Rash generalised			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Rash papular			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Scab			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Spider naevus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Itching scar			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Scar pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Umbilical discharge			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Bladder pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Cystitis noninfective			

subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Dysuria			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Glycosuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Hydronephrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 5 (0.00%)	3 / 11 (27.27%)	0 / 2 (0.00%)
occurrences (all)	0	16	0
Renal failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal tubular disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Urine flow decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Albuminuria			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nephropathy toxic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	3 / 5 (60.00%)	6 / 11 (54.55%)	1 / 2 (50.00%)
occurrences (all)	5	10	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	4 / 11 (36.36%)	0 / 2 (0.00%)
occurrences (all)	2	8	0
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Limb mass			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	2 / 5 (40.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	12	2	0
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 5 (40.00%)	4 / 11 (36.36%)	0 / 2 (0.00%)
occurrences (all)	4	10	0
Pain in jaw			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Periostitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Muscle rigidity			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye infection bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eyelid infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Gingivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	1 / 2 (50.00%)
occurrences (all)	1	0	1
Localised infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Osteomyelitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Pseudomonas infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	1 / 5 (20.00%)	2 / 11 (18.18%)	2 / 2 (100.00%)
occurrences (all)	2	3	2
Sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Staphylococcal sepsis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Vaginal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vascular device infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Abscess limb			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Anal fungal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Angular cheilitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Catheter site infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Genital candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Genital infection fungal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cachexia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	4 / 5 (80.00%)	5 / 11 (45.45%)	0 / 2 (0.00%)
occurrences (all)	14	9	0
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypermagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 11 (18.18%)	0 / 2 (0.00%)
occurrences (all)	0	4	0
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 11 (9.09%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypoproteinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperamylasaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 11 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1, Single-agent Dose-finding: Lenvatinib 17 mg/m^2	Cohort2B,Single-agentExpansion,Osteosarcoma:Lenvatinib 14mg/m^2	Cohort 2A, Single-agent Expansion, DTC: Lenvatinib 14 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	29 / 31 (93.55%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Malignant pleural effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion malignant			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	1 / 7 (14.29%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	1	4	0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	4 / 7 (57.14%)	10 / 31 (32.26%)	1 / 1 (100.00%)
occurrences (all)	12	13	2
Hypotension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Lymphoedema			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Superior vena cava syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	10 / 31 (32.26%)	0 / 1 (0.00%)
occurrences (all)	0	13	0
Axillary pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Catheter site bruise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Catheter site dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Device related thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Face oedema			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	3 / 7 (42.86%)	9 / 31 (29.03%)	0 / 1 (0.00%)
occurrences (all)	7	15	0
Inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infusion site irritation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Pain			
subjects affected / exposed	1 / 7 (14.29%)	4 / 31 (12.90%)	0 / 1 (0.00%)
occurrences (all)	1	4	0
Pyrexia			
subjects affected / exposed	4 / 7 (57.14%)	11 / 31 (35.48%)	1 / 1 (100.00%)
occurrences (all)	10	17	1
Swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injection site mass			

subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Sensation of foreign body			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Genital pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Amenorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Genital lesion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Perineal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Premature menopause			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 7 (28.57%)	9 / 31 (29.03%)	0 / 1 (0.00%)
occurrences (all)	2	10	0
Dysaesthesia pharynx			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	6 / 31 (19.35%)	0 / 1 (0.00%)
occurrences (all)	0	10	0
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)	6 / 31 (19.35%)	0 / 1 (0.00%)
occurrences (all)	2	8	0
Dyspnoea exertional			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	2 / 7 (28.57%)	4 / 31 (12.90%)	1 / 1 (100.00%)
occurrences (all)	2	7	1
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pharyngeal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Productive cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Respiratory distress			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 7 (14.29%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Depression			

subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	2
Irritability			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Major depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Mood altered			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 7 (28.57%)	1 / 31 (3.23%)	1 / 1 (100.00%)
occurrences (all)	4	1	1
Amylase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 7 (28.57%)	2 / 31 (6.45%)	1 / 1 (100.00%)
occurrences (all)	6	2	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Blood bilirubin increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood calcium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Blood magnesium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 7 (0.00%)	9 / 31 (29.03%)	1 / 1 (100.00%)
occurrences (all)	0	13	1
Blood urea increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Blood uric acid decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			

subjects affected / exposed	1 / 7 (14.29%)	4 / 31 (12.90%)	0 / 1 (0.00%)
occurrences (all)	1	4	0
Culture stool positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Full blood count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	2	5	0
Haemoglobin decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lipase decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Neutrophil count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Platelet count decreased			
subjects affected / exposed	2 / 7 (28.57%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	3	14	0
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Thyroglobulin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Thyroxine decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	3 / 7 (42.86%)	11 / 31 (35.48%)	0 / 1 (0.00%)
occurrences (all)	5	17	0
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Occult blood positive			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Thyroxine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Weight increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	2
White blood cell count increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Wound dehiscence			

subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Anaemia postoperative			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ankle fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Vaccination complication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Left ventricular dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Pericardial effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Ventricular dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Cardiac dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Cardiotoxicity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Bundle branch block right			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Systolic dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amputation stump pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cranial nerve paralysis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	1 / 1 (100.00%)
occurrences (all)	0	3	1
Dysaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 7 (42.86%)	15 / 31 (48.39%)	0 / 1 (0.00%)
occurrences (all)	6	20	0
Hypoaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Migraine			

subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Monoparesis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Phantom pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pyramidal tract syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Sensory disturbance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	4 / 31 (12.90%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Syncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Toxic encephalopathy			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Acquired antithrombin III deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	5 / 31 (16.13%)	0 / 1 (0.00%)
occurrences (all)	1	7	0
Febrile neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Polycythaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	0	7	0
Ear and labyrinth disorders			
Tinnitus			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye discharge			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye ulcer			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Papilloedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	2 / 7 (28.57%)	9 / 31 (29.03%)	1 / 1 (100.00%)
occurrences (all)	6	27	1
Abdominal pain upper			
subjects affected / exposed	1 / 7 (14.29%)	4 / 31 (12.90%)	0 / 1 (0.00%)
occurrences (all)	1	9	0
Anal fissure			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Anal fistula			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Anal incontinence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anal pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anal skin tags			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Constipation			

subjects affected / exposed	1 / 7 (14.29%)	10 / 31 (32.26%)	0 / 1 (0.00%)
occurrences (all)	1	14	0
Diarrhoea			
subjects affected / exposed	4 / 7 (57.14%)	12 / 31 (38.71%)	1 / 1 (100.00%)
occurrences (all)	8	29	12
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyschezia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	5 / 31 (16.13%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Eructation			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Flatulence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Glossitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematemesis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	3 / 7 (42.86%)	12 / 31 (38.71%)	0 / 1 (0.00%)
occurrences (all)	3	16	0
Noninfective gingivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Oesophageal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral dysaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pancreatitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Perianal erythema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Proctalgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Proctitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	4 / 31 (12.90%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	4 / 7 (57.14%)	14 / 31 (45.16%)	0 / 1 (0.00%)
occurrences (all)	5	41	0
Anal fissure haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Mouth haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			

subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	10	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	3
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Dermatitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dermatitis bullous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Eczema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Hair colour changes			

subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hyperkeratosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Onychalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	1 / 1 (100.00%)
occurrences (all)	0	2	2
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rash generalised			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	2

Rash papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Scab			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Spider naevus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Ecchymosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Itching scar			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Palmar erythema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Scar pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Umbilical discharge			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0

Purpura			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Bladder pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cystitis noninfective			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Glycosuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Hydronephrosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Leukocyturia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Proteinuria			

subjects affected / exposed	3 / 7 (42.86%)	13 / 31 (41.94%)	0 / 1 (0.00%)
occurrences (all)	8	27	0
Renal failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Renal tubular disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urine flow decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Albuminuria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Nephropathy toxic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Hypothyroidism			
subjects affected / exposed	3 / 7 (42.86%)	13 / 31 (41.94%)	0 / 1 (0.00%)
occurrences (all)	3	17	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	10 / 31 (32.26%)	0 / 1 (0.00%)
occurrences (all)	2	17	0
Back pain			
subjects affected / exposed	2 / 7 (28.57%)	10 / 31 (32.26%)	1 / 1 (100.00%)
occurrences (all)	2	15	2
Bone pain			

subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Coccydynia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Limb mass			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 7 (0.00%)	6 / 31 (19.35%)	0 / 1 (0.00%)
occurrences (all)	0	6	0
Musculoskeletal pain			
subjects affected / exposed	1 / 7 (14.29%)	10 / 31 (32.26%)	0 / 1 (0.00%)
occurrences (all)	2	14	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	1 / 1 (100.00%)
occurrences (all)	0	3	1
Pain in extremity			

subjects affected / exposed	3 / 7 (42.86%)	9 / 31 (29.03%)	0 / 1 (0.00%)
occurrences (all)	5	10	0
Pain in jaw			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Periostitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Muscle rigidity			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Eye infection bacterial			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eyelid infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	1	1	0

Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Osteomyelitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pseudomonas infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	3 / 7 (42.86%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	3	3	0
Sepsis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Staphylococcal sepsis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Vaginal infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Vascular device infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Abscess limb			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Anal fungal infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Angular cheilitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Catheter site infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Genital candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Genital infection fungal			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cachexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	3 / 7 (42.86%)	15 / 31 (48.39%)	0 / 1 (0.00%)
occurrences (all)	5	26	0
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Electrolyte imbalance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	8
Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	1 / 1 (100.00%)
occurrences (all)	0	1	2
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Hypokalaemia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Hypomagnesaemia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 31 (6.45%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Hyponatraemia			
subjects affected / exposed	1 / 7 (14.29%)	3 / 31 (9.68%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypoproteinaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperamylasaemia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 31 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	2
Hypochloraemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 31 (3.23%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Cohort 3B, Combination Expansion: Lenvatinib 14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 14 mg/m^2	Cohort 3A, Combination Dose-finding: Lenvatinib 11 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	11 / 11 (100.00%)	11 / 11 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Malignant pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pericardial effusion malignant			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Flushing			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Hypertension			
subjects affected / exposed	5 / 20 (25.00%)	5 / 11 (45.45%)	3 / 11 (27.27%)
occurrences (all)	6	10	4
Hypotension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Superior vena cava syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 20 (40.00%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	28	3	9
Axillary pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Catheter site bruise			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Catheter site dermatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			

subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Catheter site swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Device related thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Fatigue			
subjects affected / exposed	4 / 20 (20.00%)	6 / 11 (54.55%)	4 / 11 (36.36%)
occurrences (all)	4	9	8
Inflammation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infusion site irritation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Localised oedema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
Non-cardiac chest pain			

subjects affected / exposed	1 / 20 (5.00%)	3 / 11 (27.27%)	1 / 11 (9.09%)
occurrences (all)	3	4	1
Oedema peripheral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	6 / 20 (30.00%)	3 / 11 (27.27%)	6 / 11 (54.55%)
occurrences (all)	9	5	6
Swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Injection site mass			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Genital pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Menstruation irregular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal pruritus			

subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Amenorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Genital lesion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Perineal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Premature menopause			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 20 (30.00%)	4 / 11 (36.36%)	4 / 11 (36.36%)
occurrences (all)	6	5	4
Dysaesthesia pharynx			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	2	3	2
Dyspnoea			
subjects affected / exposed	2 / 20 (10.00%)	2 / 11 (18.18%)	3 / 11 (27.27%)
occurrences (all)	3	3	3
Dyspnoea exertional			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	7 / 20 (35.00%)	6 / 11 (54.55%)	5 / 11 (45.45%)
occurrences (all)	15	8	10
Hypoxia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	4 / 20 (20.00%)	4 / 11 (36.36%)	2 / 11 (18.18%)
occurrences (all)	8	4	2
Pharyngeal inflammation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
Pleural effusion			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Pleuritic pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Pneumonitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pneumothorax			
subjects affected / exposed	1 / 20 (5.00%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	1	2	1
Productive cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Respiratory distress			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Haemoptysis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 20 (0.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Anxiety			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	3 / 11 (27.27%)
occurrences (all)	2	1	8
Confusional state			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	3 / 11 (27.27%)
occurrences (all)	0	1	7
Irritability			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nightmare			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Major depression			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 20 (25.00%)	1 / 11 (9.09%)	3 / 11 (27.27%)
occurrences (all)	13	2	3
Amylase increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 20 (15.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	13	3	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	3	0	3
Blood calcium decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	1	1	2
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Blood magnesium decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	10
Blood phosphorus decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood potassium decreased			

subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	5	0	2
Blood thyroid stimulating hormone increased			
subjects affected / exposed	5 / 20 (25.00%)	0 / 11 (0.00%)	3 / 11 (27.27%)
occurrences (all)	8	0	4
Blood urea increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Blood uric acid decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Culture stool positive			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	2
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Full blood count decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	4	4	1
Haemoglobin decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Lipase decreased			

subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Lymphocyte count decreased			
subjects affected / exposed	6 / 20 (30.00%)	2 / 11 (18.18%)	4 / 11 (36.36%)
occurrences (all)	15	5	19
Neutrophil count decreased			
subjects affected / exposed	10 / 20 (50.00%)	2 / 11 (18.18%)	2 / 11 (18.18%)
occurrences (all)	46	5	2
Neutrophil count increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	11 / 20 (55.00%)	4 / 11 (36.36%)	2 / 11 (18.18%)
occurrences (all)	86	16	12
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Thyroglobulin increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Thyroxine decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Urine output decreased			
subjects affected / exposed	0 / 20 (0.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	5 / 20 (25.00%)	3 / 11 (27.27%)	6 / 11 (54.55%)
occurrences (all)	9	7	8
White blood cell count decreased			
subjects affected / exposed	13 / 20 (65.00%)	4 / 11 (36.36%)	5 / 11 (45.45%)
occurrences (all)	88	11	8

Coronavirus test positive			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Occult blood positive			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Thyroxine increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2
Contusion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2
Fall			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	2	6
Ligament sprain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Limb injury			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	2 / 20 (10.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Wound			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Wound complication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Wound dehiscence			
subjects affected / exposed	0 / 20 (0.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Anaemia postoperative			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ankle fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Left ventricular dysfunction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Sinus bradycardia			
subjects affected / exposed	0 / 20 (0.00%)	4 / 11 (36.36%)	0 / 11 (0.00%)
occurrences (all)	0	4	0
Tachycardia			
subjects affected / exposed	2 / 20 (10.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Ventricular dysfunction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Cardiac dysfunction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cardiotoxicity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bundle branch block right			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Systolic dysfunction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Amputation stump pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cranial nerve paralysis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	3 / 11 (27.27%)	1 / 11 (9.09%)
occurrences (all)	2	5	1
Dysaesthesia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Generalised tonic-clonic seizure			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	6 / 20 (30.00%)	7 / 11 (63.64%)	4 / 11 (36.36%)
occurrences (all)	10	13	5
Hypoaesthesia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Lethargy			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	2	1	2
Migraine			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	8
Monoparesis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	3	2	0
Paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Phantom pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pyramidal tract syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sciatica			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sensory disturbance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Toxic encephalopathy			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Dysgeusia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Acquired antithrombin III deficiency			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	15 / 20 (75.00%)	7 / 11 (63.64%)	9 / 11 (81.82%)
occurrences (all)	77	29	43
Febrile neutropenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	3 / 20 (15.00%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	20	21	4
Lymphopenia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	3	0	8

Neutropenia			
subjects affected / exposed	8 / 20 (40.00%)	6 / 11 (54.55%)	6 / 11 (54.55%)
occurrences (all)	51	25	19
Polycythaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	5 / 20 (25.00%)	4 / 11 (36.36%)	5 / 11 (45.45%)
occurrences (all)	46	54	50
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Vertigo			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	3	0
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Dry eye			
subjects affected / exposed	0 / 20 (0.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Eye discharge			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2
Eye ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	4
Ocular hyperaemia			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Papilloedema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	7 / 20 (35.00%)	6 / 11 (54.55%)	6 / 11 (54.55%)
occurrences (all)	23	18	20
Abdominal pain upper			
subjects affected / exposed	4 / 20 (20.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	8	1	0
Anal fissure			
subjects affected / exposed	2 / 20 (10.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Anal fistula			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Anal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Anal inflammation			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	1	1	1

Anal pruritus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Anal skin tags			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Aphthous ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	7 / 20 (35.00%)	5 / 11 (45.45%)	6 / 11 (54.55%)
occurrences (all)	10	8	11
Diarrhoea			
subjects affected / exposed	13 / 20 (65.00%)	6 / 11 (54.55%)	8 / 11 (72.73%)
occurrences (all)	72	14	24
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dyschezia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	4 / 20 (20.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Eructation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	4	0

Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Glossitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	1 / 20 (5.00%)	3 / 11 (27.27%)	0 / 11 (0.00%)
occurrences (all)	4	3	0
Haemorrhoids			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypoaesthesia oral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	0 / 20 (0.00%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	0	2	1
Nausea			
subjects affected / exposed	14 / 20 (70.00%)	8 / 11 (72.73%)	8 / 11 (72.73%)
occurrences (all)	45	28	28
Noninfective gingivitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Odynophagia			
subjects affected / exposed	2 / 20 (10.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Oesophageal obstruction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Oral discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oral dysaesthesia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	0	1	3
Oral pain			
subjects affected / exposed	1 / 20 (5.00%)	3 / 11 (27.27%)	2 / 11 (18.18%)
occurrences (all)	1	3	2
Pancreatitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Perianal erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 11 (18.18%)	3 / 11 (27.27%)
occurrences (all)	1	2	5
Proctitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	2
Stomatitis			
subjects affected / exposed	4 / 20 (20.00%)	3 / 11 (27.27%)	5 / 11 (45.45%)
occurrences (all)	8	4	7
Toothache			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	12 / 20 (60.00%)	8 / 11 (72.73%)	9 / 11 (81.82%)
occurrences (all)	58	20	28
Anal fissure haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Dermatitis acneiform			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dermatitis bullous			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dry skin			

subjects affected / exposed	0 / 20 (0.00%)	3 / 11 (27.27%)	3 / 11 (27.27%)
occurrences (all)	0	3	4
Eczema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Hair colour changes			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Hyperkeratosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Night sweats			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Onychalgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pain of skin			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 20 (0.00%)	3 / 11 (27.27%)	1 / 11 (9.09%)
occurrences (all)	0	12	1
Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	1	3	0
Rash			
subjects affected / exposed	2 / 20 (10.00%)	3 / 11 (27.27%)	3 / 11 (27.27%)
occurrences (all)	4	7	3

Rash generalised			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Rash macular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 20 (0.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
Rash papular			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Scab			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Spider naevus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Itching scar			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Palmar erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Scar pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Umbilical discharge			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Bladder pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cystitis noninfective			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 20 (5.00%)	2 / 11 (18.18%)	0 / 11 (0.00%)
occurrences (all)	2	3	0
Glycosuria			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Haematuria			
subjects affected / exposed	4 / 20 (20.00%)	1 / 11 (9.09%)	5 / 11 (45.45%)
occurrences (all)	12	2	6
Hydronephrosis			

subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	9	0	0
Pollakiuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	9 / 20 (45.00%)	5 / 11 (45.45%)	3 / 11 (27.27%)
occurrences (all)	44	13	5
Renal failure			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Renal impairment			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Renal tubular disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Urine flow decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Albuminuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nephropathy toxic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	6 / 20 (30.00%)	8 / 11 (72.73%)	6 / 11 (54.55%)
occurrences (all)	8	11	7

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 20 (15.00%)	6 / 11 (54.55%)	6 / 11 (54.55%)
occurrences (all)	8	8	7
Back pain			
subjects affected / exposed	5 / 20 (25.00%)	4 / 11 (36.36%)	6 / 11 (54.55%)
occurrences (all)	5	6	7
Bone pain			
subjects affected / exposed	3 / 20 (15.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	3	0	3
Coccydynia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Groin pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Joint swelling			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Limb mass			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Muscular weakness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			

subjects affected / exposed	3 / 20 (15.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	5	1	3
Myalgia			
subjects affected / exposed	2 / 20 (10.00%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	3	3	1
Neck pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	3 / 20 (15.00%)	5 / 11 (45.45%)	6 / 11 (54.55%)
occurrences (all)	4	11	16
Pain in jaw			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Periostitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Spinal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Muscle atrophy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscle rigidity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2

Cystitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Device related infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye infection bacterial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Eyelid infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Folliculitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2

Nasopharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Oral candidiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Oral herpes			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Osteomyelitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pseudomonas infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Rhinitis			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
Sepsis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Sinusitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Staphylococcal sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	2	0	2
Vaginal infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vascular device infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Abscess limb			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Anal fungal infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Angular cheilitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Catheter site infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Genital candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Genital infection fungal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cachexia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	7 / 20 (35.00%)	3 / 11 (27.27%)	5 / 11 (45.45%)
occurrences (all)	12	3	8
Dehydration			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	2	4	2
Electrolyte imbalance			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	4	0
Fluid retention			

subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Hypermagnesaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 11 (9.09%)	2 / 11 (18.18%)
occurrences (all)	5	1	4
Hypocalcaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Hypokalaemia			
subjects affected / exposed	3 / 20 (15.00%)	1 / 11 (9.09%)	4 / 11 (36.36%)
occurrences (all)	10	4	8
Hypomagnesaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	4
Hyponatraemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Hypophosphataemia			
subjects affected / exposed	4 / 20 (20.00%)	2 / 11 (18.18%)	3 / 11 (27.27%)
occurrences (all)	12	13	8
Hypoproteinaemia			

subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Metabolic acidosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	0 / 20 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperamylasaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2014	Details added to define Grade 4 hypertension. Change in ANC level in inclusion criteria. Contraceptive period was extended in the inclusion criteria. Management of PRES added to Treatment section.
14 April 2015	Secondary objective of observing bone growth changed to assessing palatability and acceptability of study drug. Details added to dose escalation procedures for single-agent lenvatinib and combination therapy. Dose-escalation method changed from Continual-reassessment method (CRM) to Time-to-event continual-reassessment method (TiTE-CRM). Use of eastern cooperative oncology group performance status (ECOG PS) changed to karnofsky performance status (KPS). Previous treatment with ifosfamide and neurotoxicity added to exclusion criteria. Run-In Period added for subjects aged 2 to <6 years in Cohort 1. Details added for management of toxicity for subjects receiving combination therapy. Updates to study drug administration and permitted concomitant medications. Measurement of tibial growth plates and fecal occult blood tests added to baseline assessments.
01 September 2016	Different standards set for hematologic toxicity for subjects receiving combination therapy. RD for single-agent lenvatinib in Cohort 1 determined as 14 mg/m^2, with a maximum lenvatinib dosage of 24 mg daily. Procedures added for study drug administration when subject underwent surgery. Details added regarding frequency of tumor assessments. Exploratory endpoint of OS added. Estimated number of enrolled subjects with radioiodine-131 (I131)-refractory differentiated thyroid cancer (RR-DTC) reduced and subjects with osteosarcoma increased. Permitted enrollment of subjects with RR-DTC and osteosarcoma subjects in Cohort 2A and 2B, respectively, who had either measurable or evaluable disease (based on RECIST 1.1). Sites of tumor assessments were updated for subjects with RR-DTC and osteosarcoma as advised by the protocol steering committee (PSC), to align with the standard of care.
12 November 2019	OS changed from an exploratory to a secondary objective. Clarified the procedure for procurement of study drug for subjects continuing study treatment at the time of the data cutoff date for the primary analysis. Clarified the timing for collection of blood samples for pharmacodynamic and biomarker analysis for subjects ongoing after the data cutoff date for the primary analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported