Clinical trial results:
AN OPEN-LABEL, DOSE-FINDING AND PROOF OF CONCEPT STUDY OF THE PD-L1 PROBODY® THERAPEUTIC, CX-072, AS MONOTHERAPY AND IN COMBINATION WITH YERVOY® (IPILIMUMAB) OR WITH ZELBORAF® (VEMURAFENIB) IN SUBJECTS WITH ADVANCED OR RECURRENT SOLID TUMORS OR LYMPHOMAS

Summary

EudraCT number	2016-002490-36
Trial protocol	HU ES NL PL GB
Global end of trial date	27 October 2020

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	CTMX-M-072-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03013491
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CytomX Therapeutics, Inc
Sponsor organisation address	151 Oyster Point Boulevard, Suite 400, South San Francisco, United States, 94080
Public contact	Head of Clinical Operations, CytomX Therapeutics, Inc, +1 650-515-3185, Clinicaltrials@cytomx.com
Scientific contact	Head of Clinical Operations, CytomX Therapeutics, Inc, +1 650-515-3185, Clinicaltrials@cytomx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 October 2020
Global end of trial reached?	Yes
Global end of trial date	27 October 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Parts A through C:
1. To evaluate the safety and tolerability of multiple doses of CX-072 administered as monotherapy or in combination with ipilimumab or vemurafenib to patients with metastatic or locally advanced unresectable solid tumors or lymphomas;
2. To determine the maximum tolerated dose (MTD) and dose-limiting toxicities (DLTs) of the following:
• CX-072 as a monotherapy administered to programmed cell death 1/programmed cell death ligand 1 (PD-1/PD-L1) naive patients.
• CX-072 in combination with ipilimumab administered to PD-1/PD-L1 and CTLA-4 inhibitor naïve patients.
• CX-072 in combination with ipilimumab administered to patients who had prior treatment with a PD-1/PD-L1 inhibitor.
• CX-072 in combination with vemurafenib administered to PD-1/PD-L1 naive patients
Parts D and E:
1. To obtain preliminary and confirmatory evidence of the efficacy of CX-072 monotherapy, respectively, via the objective response rate (ORR) according to the Response Evaluation Criteria

Protection of trial subjects:

All considerations regarding the protection of human subjects were carried out in accordance with the protocol, GCP, ICH Guidelines, the ethical principles that have their origin in the Declaration of Helsinki, and all applicable regulatory requirements. The investigator (according to applicable regulatory requirements) or a person designated by the investigator and under the investigator’s responsibility fully informed patients of all pertinent aspects of the clinical trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 January 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason, Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ukraine: 9
Country: Number of subjects enrolled	United States: 100
Country: Number of subjects enrolled	Netherlands: 22
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 28
Country: Number of subjects enrolled	United Kingdom: 36

Worldwide total number of subjects	196
EEA total number of subjects	51

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	136
From 65 to 84 years	60
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter study with a total of 41 sites in 6 countries (Netherlands, Poland, Spain, Ukraine, UK, and the US). A total of 278 patients were screened for the study, and 196 patients received study treatment.

Pre-assignment

Screening details:

All patients must have had histologically confirmed diagnosis of metastatic or locally advanced unresectable tumors that progressed or were intolerant to standard therapy. Patients who fulfilled the specific inclusion/exclusion criteria for one of the Parts (A, A2, B1, B2, C or D) at the screening visit were eligible for admission into the study.

Period 1

Period 1 title	Parts A, A2, B1, B2, C and D
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A and Part A2 - CX-072 0.03 mg/kg

Arm description:

Part A and Part A2 - Monotherapy CX-072 0.03 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg.

Arm title	Part A and Part A2 - CX-072 0.1 mg/kg

Arm description:

Part A and Part A2 - Monotherapy CX-072 0.1 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg

Arm title	Part A and Part A2 - CX-072 0.3 mg/kg

Arm description:

Part A and Part A2 - Monotherapy CX-072 0.3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg

Arm title	Part A and Part A2 - CX-072 1 mg/kg

Arm description:

Part A and Part A2 - Monotherapy CX-072 1 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg

Arm title	Part A and Part A2 - CX-072 3 mg/kg

Arm description:

Part A and Part A2 - Monotherapy CX-072 3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg.

Arm title	Part A and Part A2 - CX-072 10 mg/kg

Arm description:

Part A and Part A2 - Monotherapy CX-072 10 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg

Arm title	Part A and Part A2 - CX-072 30 mg/kg

Arm description:

Part A and Part A2 - Monotherapy CX-072 30 mg/kg

Arm type	Experimental

Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg.

Arm title	Part B1 – CX-072 0.3 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Part B1 - Combination CX-072 0.3 mg/kg + ipilimumab 3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 0.3, 1, 3, and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at the following doses: 3, 6, and 10 mg/kg.

Arm title	Part B1 – CX-072 1 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Part B1 - Combination CX-072 1 mg/kg + ipilimumab 3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 0.3, 1, 3, and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at the following doses: 3, 6, and 10 mg/kg.

Arm title	Part B1 – CX-072 3 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Part B1 - Combination CX-072 3 mg/kg + ipilimumab 3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 0.3, 1, 3, and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at the following doses: 3, 6, and 10 mg/kg.

Arm title	Part B1 – CX-072 10 mg/kg + Ipilimumab 3 mg/kg

Arm description:

Part B1 - Combination CX-072 10 mg/kg + ipilimumab 3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 0.3, 1, 3, and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at the following doses: 3, 6, and 10 mg/kg.

Arm title	Part B1 – CX-072 10 mg/kg + Ipilimumab 6 mg/kg

Arm description:

Part B1 - Combination CX-072 10 mg/kg + ipilimumab 6 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 0.3, 1, 3, and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy

Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at the following doses: 3, 6, and 10 mg/kg.

Arm title	Part B1 – CX-072 10 mg/kg + Ipilimumab 10 mg/kg

Arm description:

Part B1 - Combination CX-072 10 mg/kg + ipilimumab 10 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 0.3, 1, 3, and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at 3 mg/kg.

Arm title	Part B2 – CX-072 3 mg/kg + ipilimumab 3 mg/kg

Arm description:

Part B2 - Combination CX-072 3 mg/kg + ipilimumab 3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 3 and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at 3 mg/kg.

Arm title	Part B2 – CX-072 10 mg/kg + ipilimumab 3 mg/kg

Arm description:

Part B2 - Combination CX-072 10 mg/kg + ipilimumab 3 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 3 and 10 mg/kg

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	Yervoy
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Yervoy (Ipilimumab) is supplied in single-use vials of 50 mg/10 mL and 200 mg/40 mL.

Participants received escalating doses of CX-072 administered concomitantly with ipilimumab. Ipilimumab was administered intravenously (IV) at 3 mg/kg.

Arm title	Part C - CX-072 1 mg/kg + Vemurafenib 960 mg

Arm description:

Part C - Combination CX-072 1 mg/kg + Vemurafenib 960 mg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 1, 3 and 10 mg/kg

Investigational medicinal product name	Vemurafenib
Investigational medicinal product code	
Other name	Zelboraf
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vemurafenib is available as 240 mg tablets for oral use. Tablets are white to off-white and are supplied as 240 mg film-coated tablets with VEM debossed on 1 side.

Vemurafenib is administered PO, twice daily (approximately every 12 hours [q12h]) at 960 mg.

Arm title	Part C - CX-072 3 mg/kg + Vemurafenib 960 mg

Arm description:

Part C - Combination CX-072 3 mg/kg + Vemurafenib 960 mg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 1, 3 and 10 mg/kg

Investigational medicinal product name	Vemurafenib
Investigational medicinal product code	
Other name	Zelboraf
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vemurafenib is available as 240 mg tablets for oral use. Tablets are white to off-white and are supplied as 240 mg film-coated tablets with VEM debossed on 1 side.

Vemurafenib is administered PO, twice daily (approximately every 12 hours [q12h]) at 960 mg.

Arm title	Part C - CX-072 10 mg/kg + Vemurafenib 960 mg

Arm description:

Part C - Combination CX-072 10 mg/kg + Vemurafenib 960 mg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 was administered intravenously (IV) at the following doses: 1, 3, and 10 mg/kg

Investigational medicinal product name	Vemurafenib
Investigational medicinal product code	
Other name	Zelboraf
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vemurafenib is available as 240 mg tablets for oral use.
Tablets are white to off-white and are supplied as 240 mg film-coated tablets with VEM debossed on 1 side.

Arm title	Part D - CX-072 10 mg/kg

Arm description:

Part D - Monotherapy CX-072 10 mg/kg

Arm type	Experimental
Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at 10 mg/kg

Number of subjects in period 1	Part A and Part A2 - CX-072 0.03 mg/kg	Part A and Part A2 - CX-072 0.1 mg/kg	Part A and Part A2 - CX-072 0.3 mg/kg
Started	2	2	8
Completed	0	0	0
Not completed	2	2	8
Adverse event, serious fatal	2	2	5
Consent withdrawn by subject	-	-	-

Other	-	-	-
Termination of Study by Sponsor	-	-	2
Lost to follow-up	-	-	1

Number of subjects in period 1	Part A and Part A2 - CX-072 1 mg/kg	Part A and Part A2 - CX-072 3 mg/kg	Part A and Part A2 - CX-072 10 mg/kg
Started	9	13	16
Completed	1	0	0
Not completed	8	13	16
Adverse event, serious fatal	3	9	12
Consent withdrawn by subject	4	2	1
Other	1	-	1
Termination of Study by Sponsor	-	1	2
Lost to follow-up	-	1	-

Number of subjects in period 1	Part A and Part A2 - CX-072 30 mg/kg	Part B1 – CX-072 0.3 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 1 mg/kg + Ipilimumab 3 mg/kg
Started	3	6	3
Completed	0	1	0
Not completed	3	5	3
Adverse event, serious fatal	3	5	1
Consent withdrawn by subject	-	-	-
Other	-	-	1
Termination of Study by Sponsor	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Part B1 – CX-072 3 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 10 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 10 mg/kg + Ipilimumab 6 mg/kg
Started	3	8	6
Completed	0	0	0
Not completed	3	8	6
Adverse event, serious fatal	2	4	1
Consent withdrawn by subject	-	1	2
Other	-	2	1
Termination of Study by Sponsor	1	1	2
Lost to follow-up	-	-	-

Number of subjects in period 1	Part B1 – CX-072 10 mg/kg + Ipilimumab 10 mg/kg	Part B2 – CX-072 3 mg/kg + ipilimumab 3 mg/kg	Part B2 – CX-072 10 mg/kg + ipilimumab 3 mg/kg
Started	1	6	1
Completed	0	0	1
Not completed	1	6	0
Adverse event, serious fatal	1	4	-
Consent withdrawn by subject	-	2	-

Other	-	-	-
Termination of Study by Sponsor	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Part C - CX-072 1 mg/kg + Vemurafenib 960 mg	Part C - CX-072 3 mg/kg + Vemurafenib 960 mg	Part C - CX-072 10 mg/kg + Vemurafenib 960 mg
Started	3	6	2
Completed	0	1	0
Not completed	3	5	2
Adverse event, serious fatal	3	5	1
Consent withdrawn by subject	-	-	-
Other	-	-	-
Termination of Study by Sponsor	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Part D - CX-072 10 mg/kg
Started	98
Completed	11
Not completed	87
Adverse event, serious fatal	47
Consent withdrawn by subject	18
Other	6
Termination of Study by Sponsor	13
Lost to follow-up	3

Period 2

Period 2 title	Long-Term extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Long-Term extension

Arm description:

Participants from Study CTMX-M-072-001 were eligible to enroll in the LTE if they were actively receiving CX-072 monotherapy and would continue to benefit from treatment with CX-072 monotherapy as determined by the Investigator.

Patients continued the same dose of CX-072 that they last received in the previous cohort (Parts A-D) of the study that they were enrolled in. No dose increase or decrease of CX-072 was permitted in long-term extension.

Arm type	Experimental

Investigational medicinal product name	CX-072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

CX-072 monotherapy was administered intravenously (IV) at the following doses: 0.03, 0.1, 0.3, 1, 3, 10, and 30 mg/kg

Number of subjects in period 2	Long-Term extension
Started	15
Completed	10
Not completed	5
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Disease Progression	2

Baseline characteristics

Reporting groups

Reporting group title	Part A and Part A2 - CX-072 0.03 mg/kg

Reporting group description:

Part A and Part A2 - Monotherapy CX-072 0.03 mg/kg

Reporting group title	Part A and Part A2 - CX-072 0.1 mg/kg

Reporting group description:

Part A and Part A2 - Monotherapy CX-072 0.1 mg/kg

Reporting group title	Part A and Part A2 - CX-072 0.3 mg/kg

Reporting group description:

Part A and Part A2 - Monotherapy CX-072 0.3 mg/kg

Reporting group title	Part A and Part A2 - CX-072 1 mg/kg

Reporting group description:

Part A and Part A2 - Monotherapy CX-072 1 mg/kg

Reporting group title	Part A and Part A2 - CX-072 3 mg/kg

Reporting group description:

Part A and Part A2 - Monotherapy CX-072 3 mg/kg

Reporting group title	Part A and Part A2 - CX-072 10 mg/kg

Reporting group description:

Part A and Part A2 - Monotherapy CX-072 10 mg/kg

Reporting group title	Part A and Part A2 - CX-072 30 mg/kg

Reporting group description:

Part A and Part A2 - Monotherapy CX-072 30 mg/kg

Reporting group title	Part B1 – CX-072 0.3 mg/kg + Ipilimumab 3 mg/kg

Reporting group description:

Part B1 - Combination CX-072 0.3 mg/kg + ipilimumab 3 mg/kg

Reporting group title	Part B1 – CX-072 1 mg/kg + Ipilimumab 3 mg/kg

Reporting group description:

Part B1 - Combination CX-072 1 mg/kg + ipilimumab 3 mg/kg

Reporting group title	Part B1 – CX-072 3 mg/kg + Ipilimumab 3 mg/kg

Reporting group description:

Part B1 - Combination CX-072 3 mg/kg + ipilimumab 3 mg/kg

Reporting group title	Part B1 – CX-072 10 mg/kg + Ipilimumab 3 mg/kg

Reporting group description:

Part B1 - Combination CX-072 10 mg/kg + ipilimumab 3 mg/kg

Reporting group title	Part B1 – CX-072 10 mg/kg + Ipilimumab 6 mg/kg

Reporting group description:

Part B1 - Combination CX-072 10 mg/kg + ipilimumab 6 mg/kg

Reporting group title	Part B1 – CX-072 10 mg/kg + Ipilimumab 10 mg/kg

Reporting group description:

Part B1 - Combination CX-072 10 mg/kg + ipilimumab 10 mg/kg

Reporting group title	Part B2 – CX-072 3 mg/kg + ipilimumab 3 mg/kg

Reporting group description:

Part B2 - Combination CX-072 3 mg/kg + ipilimumab 3 mg/kg

Reporting group title	Part B2 – CX-072 10 mg/kg + ipilimumab 3 mg/kg

Reporting group description:
Part B2 - Combination CX-072 10 mg/kg + ipilimumab 3 mg/kg

Reporting group title	Part C - CX-072 1 mg/kg + Vemurafenib 960 mg
Reporting group description: Part C - Combination CX-072 1 mg/kg + Vemurafenib 960 mg	

Reporting group title	Part C - CX-072 3 mg/kg + Vemurafenib 960 mg
Reporting group description: Part C - Combination CX-072 3 mg/kg + Vemurafenib 960 mg	

Reporting group title	Part C - CX-072 10 mg/kg + Vemurafenib 960 mg
Reporting group description: Part C - Combination CX-072 10 mg/kg + Vemurafenib 960 mg	

Reporting group title	Part D - CX-072 10 mg/kg
Reporting group description: Part D - Monotherapy CX-072 10 mg/kg	

Reporting group values	Part A and Part A2 - CX-072 0.03 mg/kg	Part A and Part A2 - CX-072 0.1 mg/kg	Part A and Part A2 - CX-072 0.3 mg/kg
Number of subjects	2	2	8
Age categorical Units: Subjects			
Adults (18-64 years)	0	0	4
From 65-84 years	2	2	4
Age continuous Units: years			
arithmetic mean	69.5	72.0	60.8
standard deviation	± 2.12	± 2.83	± 9.88
Gender categorical Units: Subjects			
Female	1	2	4
Male	1	0	4

Reporting group values	Part A and Part A2 - CX-072 1 mg/kg	Part A and Part A2 - CX-072 3 mg/kg	Part A and Part A2 - CX-072 10 mg/kg
Number of subjects	9	13	16
Age categorical Units: Subjects			
Adults (18-64 years)	6	6	13
From 65-84 years	3	7	3
Age continuous Units: years			
arithmetic mean	59.2	63.3	55.3
standard deviation	± 9.43	± 15.12	± 13.11
Gender categorical Units: Subjects			
Female	3	8	9
Male	6	5	7

Reporting group values	Part A and Part A2 - CX-072 30 mg/kg	Part B1 – CX-072 0.3 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 1 mg/kg + Ipilimumab 3 mg/kg

Number of subjects	3	6	3
Age categorical Units: Subjects			
Adults (18-64 years)	3	3	3
From 65-84 years	0	3	0
Age continuous Units: years			
arithmetic mean	58.0	56.5	38.0
standard deviation	± 10.44	± 16.94	± 1.73
Gender categorical Units: Subjects			
Female	1	2	1
Male	2	4	2

Reporting group values	Part B1 – CX-072 3 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 10 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 10 mg/kg + Ipilimumab 6 mg/kg
Number of subjects	3	8	6
Age categorical Units: Subjects			
Adults (18-64 years)	3	8	6
From 65-84 years	0	0	0
Age continuous Units: years			
arithmetic mean	53.0	53.9	51.8
standard deviation	± 8.72	± 9.14	± 10.19
Gender categorical Units: Subjects			
Female	3	6	3
Male	0	2	3

Reporting group values	Part B1 – CX-072 10 mg/kg + Ipilimumab 10 mg/kg	Part B2 – CX-072 3 mg/kg + ipilimumab 3 mg/kg	Part B2 – CX-072 10 mg/kg + ipilimumab 3 mg/kg
Number of subjects	1	6	1
Age categorical Units: Subjects			
Adults (18-64 years)	0	5	1
From 65-84 years	1	1	0
Age continuous Units: years			
arithmetic mean	67.0	56.7	40
standard deviation	± 0.0	± 8.38	± 0.0
Gender categorical Units: Subjects			
Female	1	4	1
Male	0	2	0

Reporting group values	Part C - CX-072 1 mg/kg + Vemurafenib 960 mg	Part C - CX-072 3 mg/kg + Vemurafenib 960 mg	Part C - CX-072 10 mg/kg + Vemurafenib 960 mg
Number of subjects	3	6	2

Age categorical Units: Subjects			
Adults (18-64 years)	2	5	2
From 65-84 years	1	1	0
Age continuous Units: years			
arithmetic mean	47.3	46.3	53.5
standard deviation	± 17.24	± 20.88	± 9.19
Gender categorical Units: Subjects			
Female	2	4	1
Male	1	2	1

Reporting group values	Part D - CX-072 10 mg/kg	Total	
Number of subjects	98	196	
Age categorical Units: Subjects			
Adults (18-64 years)	66	136	
From 65-84 years	32	60	
Age continuous Units: years			
arithmetic mean	59.9		
standard deviation	± 12.28	-	
Gender categorical Units: Subjects			
Female	60	116	
Male	38	80	

End points

End points reporting groups

Reporting group title	Part A and Part A2 - CX-072 0.03 mg/kg
Reporting group description: Part A and Part A2 - Monotherapy CX-072 0.03 mg/kg	

Reporting group title	Part A and Part A2 - CX-072 0.1 mg/kg
Reporting group description: Part A and Part A2 - Monotherapy CX-072 0.1 mg/kg	

Reporting group title	Part A and Part A2 - CX-072 0.3 mg/kg
Reporting group description: Part A and Part A2 - Monotherapy CX-072 0.3 mg/kg	

Reporting group title	Part A and Part A2 - CX-072 1 mg/kg
Reporting group description: Part A and Part A2 - Monotherapy CX-072 1 mg/kg	

Reporting group title	Part A and Part A2 - CX-072 3 mg/kg
Reporting group description: Part A and Part A2 - Monotherapy CX-072 3 mg/kg	

Reporting group title	Part A and Part A2 - CX-072 10 mg/kg
Reporting group description: Part A and Part A2 - Monotherapy CX-072 10 mg/kg	

Reporting group title	Part A and Part A2 - CX-072 30 mg/kg
Reporting group description: Part A and Part A2 - Monotherapy CX-072 30 mg/kg	

Reporting group title	Part B1 – CX-072 0.3 mg/kg + Ipilimumab 3 mg/kg
Reporting group description: Part B1 - Combination CX-072 0.3 mg/kg + ipilimumab 3 mg/kg	

Reporting group title	Part B1 – CX-072 1 mg/kg + Ipilimumab 3 mg/kg
Reporting group description: Part B1 - Combination CX-072 1 mg/kg + ipilimumab 3 mg/kg	

Reporting group title	Part B1 – CX-072 3 mg/kg + Ipilimumab 3 mg/kg
Reporting group description: Part B1 - Combination CX-072 3 mg/kg + ipilimumab 3 mg/kg	

Reporting group title	Part B1 – CX-072 10 mg/kg + Ipilimumab 3 mg/kg
Reporting group description: Part B1 - Combination CX-072 10 mg/kg + ipilimumab 3 mg/kg	

Reporting group title	Part B1 – CX-072 10 mg/kg + Ipilimumab 6 mg/kg
Reporting group description: Part B1 - Combination CX-072 10 mg/kg + ipilimumab 6 mg/kg	

Reporting group title	Part B1 – CX-072 10 mg/kg + Ipilimumab 10 mg/kg
Reporting group description: Part B1 - Combination CX-072 10 mg/kg + ipilimumab 10 mg/kg	

Reporting group title	Part B2 – CX-072 3 mg/kg + ipilimumab 3 mg/kg
Reporting group description: Part B2 - Combination CX-072 3 mg/kg + ipilimumab 3 mg/kg	

Reporting group title	Part B2 – CX-072 10 mg/kg + ipilimumab 3 mg/kg

Reporting group description:

Part B2 - Combination CX-072 10 mg/kg + ipilimumab 3 mg/kg

Reporting group title	Part C - CX-072 1 mg/kg + Vemurafenib 960 mg

Reporting group description:

Part C - Combination CX-072 1 mg/kg + Vemurafenib 960 mg

Reporting group title	Part C - CX-072 3 mg/kg + Vemurafenib 960 mg

Reporting group description:

Part C - Combination CX-072 3 mg/kg + Vemurafenib 960 mg

Reporting group title	Part C - CX-072 10 mg/kg + Vemurafenib 960 mg

Reporting group description:

Part C - Combination CX-072 10 mg/kg + Vemurafenib 960 mg

Reporting group title	Part D - CX-072 10 mg/kg

Reporting group description:

Part D - Monotherapy CX-072 10 mg/kg

Reporting group title	Long-Term extension

Reporting group description:

Participants from Study CTMX-M-072-001 were eligible to enroll in the LTE if they were actively receiving CX-072 monotherapy and would continue to benefit from treatment with CX-072 monotherapy as determined by the Investigator.

Patients continued the same dose of CX-072 that they last received in the previous cohort (Parts A-D) of the study that they were enrolled in. No dose increase or decrease of CX-072 was permitted in long-term extension.

Primary: The Number of Subjects Experiencing a Dose Limiting Toxicity (DLT) at Various Dose Levels When Given Multiple Doses of CX-072 as a Monotherapy or in Combination With Ipilimumab or Vemurafenib

End point title	The Number of Subjects Experiencing a Dose Limiting Toxicity (DLT) at Various Dose Levels When Given Multiple Doses of CX-072 as a Monotherapy or in Combination With Ipilimumab or Vemurafenib[1][2]

End point description:

Adverse events (AEs) that were considered DLTs:
• Grade 5 AEs
• Grade 4 AEs judged by the Investigator to be treatment-related or judged by the Sponsor as a DLT, regardless of
Investigator-attribution (with some exceptions)
• Any Grade 4 endocrinopathy.
• Grade 3 AEs judged by the Investigator to be treatment-related or by the Sponsor, regardless of Investigator attribution
(with some exceptions)
• Any Grade 3 central nervous system event, regardless of duration or reversibility.
• Grade 2 pneumonitis necessitating CX-072 discontinuation
• Grade 2 ocular toxicity necessitating CX-072 discontinuation

The analysis was performed on the safety analysis population which including all enrolled subjects who received at least one dose of study drug. The baseline population and safety analysis populations are the same.

End point type	Primary

End point timeframe:

28 days (dose limiting toxicity period)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis were tested. A summary of the results has been added in the Endpoint description.

[2] - 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: This endpoint was assessed only in Parts A, B and C.

End point values	Part A and Part A2 - CX-072 0.03 mg/kg	Part A and Part A2 - CX-072 0.1 mg/kg	Part A and Part A2 - CX-072 0.3 mg/kg	Part A and Part A2 - CX-072 1 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	2	8	9
Units: patients	0	0	0	1

End point values	Part A and Part A2 - CX-072 3 mg/kg	Part A and Part A2 - CX-072 10 mg/kg	Part A and Part A2 - CX-072 30 mg/kg	Part B1 – CX-072 0.3 mg/kg + Ipilimumab 3 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	16	3	6
Units: patients	1	0	0	1

End point values	Part B1 – CX-072 1 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 3 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 10 mg/kg + Ipilimumab 3 mg/kg	Part B1 – CX-072 10 mg/kg + Ipilimumab 6 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	8	6
Units: patients	0	0	0	2

End point values	Part B1 – CX-072 10 mg/kg + Ipilimumab 10 mg/kg	Part B2 – CX-072 3 mg/kg + ipilimumab 3 mg/kg	Part B2 – CX-072 10 mg/kg + ipilimumab 3 mg/kg	Part C - CX-072 1 mg/kg + Vemurafenib 960 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	6	1	3
Units: patients	1	0	0	0

End point values	Part C - CX-072 3 mg/kg + Vemurafenib 960 mg	Part C - CX-072 10 mg/kg + Vemurafenib 960 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	2		
Units: patients	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Subjects Experiencing Anti-cancer Activity (ORR) When Given 10 mg/kg CX-072 as Monotherapy

End point title	The Percentage of Subjects Experiencing Anti-cancer Activity (ORR) When Given 10 mg/kg CX-072 as Monotherapy[3]

End point description:

The primary efficacy endpoint, ORR, was defined as the proportion of subjects with complete response (CR) or partial response (PR) on two consecutive tumor assessments according to RECIST v1.1.
Per CX-072-001 Statistical Analysis Plan, efficacy analyses will be limited to subjects who received 10 mg/kg CX-072 monotherapy during the study. This efficacy subset includes subjects from Parts A, A2 and D. Efficacy summaries will have parts A and A2 combined.

End point type	Secondary

End point timeframe:

2 years

Notes:

[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: The analysis for this endpoint is presented for patients who received the dose of 10 mg/kg of CX-072 in Parts A, A2, and D.

End point values	Part A and Part A2 - CX-072 10 mg/kg	Part D - CX-072 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	98		
Units: patients	1	13		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 2 years. Adverse event monitoring starts from the time the patient consents to the study until they complete the trial.

Adverse event reporting additional description:

AEs are presented for the treatment-emergent adverse event (TEAE) population. On-study deaths reported as SAEs due to progressive disease and considered unrelated to study drug were excluded from TEAE analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Safety Population- Part A-A2

Reporting group description:

CX-072 as Monotherapy.

Reporting group title	Safety Population- Part B1

Reporting group description:

CX-072 in combination with Ipilimumab.

Reporting group title	Safety Population- Part B2

Reporting group description:

CX-072 in combination with Ipilimumab.

Reporting group title	Safety Population- Part C

Reporting group description:

CX-072 in combination with Vemurafenib

Reporting group title	Safety Population- Part D

Reporting group description:

CX-072 10 mg/kg as monotherapy.
Dose expansion in patients with specific cancer tumor types.

Serious adverse events	Safety Population- Part A-A2	Safety Population- Part B1	Safety Population- Part B2
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 53 (39.62%)	13 / 27 (48.15%)	3 / 7 (42.86%)
number of deaths (all causes)	38	15	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			

subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour obstruction			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 27 (3.70%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 53 (1.89%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			

subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
immune-mediated pneumonitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 53 (3.77%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Clavicle fracture			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			

subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Guillain-Barre syndrome			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 53 (0.00%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 53 (3.77%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocutaneous fistula			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	1 / 53 (1.89%)	1 / 27 (3.70%)	0 / 7 (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
Small intestinal obstruction			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (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
Vomiting			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (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
Abdominal pain			
subjects affected / exposed	0 / 53 (0.00%)	6 / 27 (22.22%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 27 (7.41%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatobiliary disorders			
Hyperbilirubinaemia			

subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemobilia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	2 / 53 (3.77%)	0 / 27 (0.00%)	0 / 7 (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
Abdominal wall abscess			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (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
Respiratory tract infection			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (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
Cellulitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Safety Population-Part C	Safety Population-Part D	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 11 (72.73%)	33 / 98 (33.67%)	
number of deaths (all causes)	9	50	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			

subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour obstruction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			

subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
immune-mediated pneumonitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Guillain-Barre syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood loss anaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			

subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			

subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemobilia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endocrine disorders			
Hypophysitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	3 / 98 (3.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			

subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	4 / 98 (4.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Safety Population-Part A-A2	Safety Population-Part B1	Safety Population-Part B2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 53 (100.00%)	26 / 27 (96.30%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Infected neoplasm			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin papilloma			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metastases to meninges			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Papilloma			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 53 (5.66%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	3	1	0
Embolism			
subjects affected / exposed	0 / 53 (0.00%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Hypertension			
subjects affected / exposed	2 / 53 (3.77%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Lymphostasis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	16 / 53 (30.19%)	8 / 27 (29.63%)	2 / 7 (28.57%)
occurrences (all)	21	14	6
Pyrexia			
subjects affected / exposed	7 / 53 (13.21%)	3 / 27 (11.11%)	1 / 7 (14.29%)
occurrences (all)	10	3	2
Asthenia			
subjects affected / exposed	4 / 53 (7.55%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	4	3	0
Non-cardiac chest pain			
subjects affected / exposed	4 / 53 (7.55%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	7	0	0
Oedema peripheral			
subjects affected / exposed	5 / 53 (9.43%)	3 / 27 (11.11%)	1 / 7 (14.29%)
occurrences (all)	9	5	1
Malaise			
subjects affected / exposed	1 / 53 (1.89%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Influenza like illness			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	7	0	1
Localised oedema			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Oedema			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Peripheral swelling			
subjects affected / exposed	2 / 53 (3.77%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Chest pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			

Erectile dysfunction			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Vaginal discharge			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 53 (24.53%)	4 / 27 (14.81%)	1 / 7 (14.29%)
occurrences (all)	14	6	1
Dyspnoea			
subjects affected / exposed	9 / 53 (16.98%)	4 / 27 (14.81%)	0 / 7 (0.00%)
occurrences (all)	11	7	0
Epistaxis			
subjects affected / exposed	3 / 53 (5.66%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Productive cough			
subjects affected / exposed	1 / 53 (1.89%)	4 / 27 (14.81%)	0 / 7 (0.00%)
occurrences (all)	3	4	0
Oropharyngeal pain			
subjects affected / exposed	1 / 53 (1.89%)	3 / 27 (11.11%)	1 / 7 (14.29%)
occurrences (all)	1	3	1
Dysphonia			
subjects affected / exposed	2 / 53 (3.77%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	2	3	0
Haemoptysis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Pleural effusion			
subjects affected / exposed	0 / 53 (0.00%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 53 (5.66%)	3 / 27 (11.11%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Depression			

subjects affected / exposed	1 / 53 (1.89%)	3 / 27 (11.11%)	0 / 7 (0.00%)
occurrences (all)	1	4	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	6 / 53 (11.32%)	4 / 27 (14.81%)	1 / 7 (14.29%)
occurrences (all)	7	4	1
Alanine aminotransferase increased			
subjects affected / exposed	2 / 53 (3.77%)	5 / 27 (18.52%)	1 / 7 (14.29%)
occurrences (all)	3	9	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 53 (1.89%)	6 / 27 (22.22%)	1 / 7 (14.29%)
occurrences (all)	2	9	3
Amylase increased			
subjects affected / exposed	1 / 53 (1.89%)	4 / 27 (14.81%)	0 / 7 (0.00%)
occurrences (all)	3	8	0
Blood creatinine increased			
subjects affected / exposed	0 / 53 (0.00%)	3 / 27 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Lipase increased			
subjects affected / exposed	0 / 53 (0.00%)	3 / 27 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	5	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 53 (3.77%)	2 / 27 (7.41%)	1 / 7 (14.29%)
occurrences (all)	2	2	2
Blood bilirubin increased			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	1 / 7 (14.29%)
occurrences (all)	0	1	5
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Blood lactate dehydrogenase increased			

subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Protein total decreased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	3 / 53 (5.66%)	1 / 27 (3.70%)	2 / 7 (28.57%)
occurrences (all)	5	1	3
Blood albumin decreased			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	10 / 53 (18.87%)	4 / 27 (14.81%)	0 / 7 (0.00%)
occurrences (all)	26	5	0
Ligament sprain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Poisoning			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sunburn			

subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 53 (13.21%)	6 / 27 (22.22%)	2 / 7 (28.57%)
occurrences (all)	8	13	2
Dizziness			
subjects affected / exposed	6 / 53 (11.32%)	2 / 27 (7.41%)	1 / 7 (14.29%)
occurrences (all)	6	2	1
Neuropathy peripheral			
subjects affected / exposed	3 / 53 (5.66%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	3	2	0
Paraesthesia			
subjects affected / exposed	2 / 53 (3.77%)	1 / 27 (3.70%)	1 / 7 (14.29%)
occurrences (all)	3	1	1
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Complex regional pain syndrome			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Facial paresis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolic encephalopathy			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Taste disorder			

subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vascular encephalopathy			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	12 / 53 (22.64%)	6 / 27 (22.22%)	2 / 7 (28.57%)
occurrences (all)	15	6	2
Lymph node pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Blood loss anaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymph node haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymphocytosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Deafness unilateral			

subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Deafness neurosensory			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Keratitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	14 / 53 (26.42%)	13 / 27 (48.15%)	4 / 7 (57.14%)
occurrences (all)	19	21	4
Constipation			
subjects affected / exposed	12 / 53 (22.64%)	5 / 27 (18.52%)	0 / 7 (0.00%)
occurrences (all)	12	5	0
Diarrhoea			
subjects affected / exposed	6 / 53 (11.32%)	7 / 27 (25.93%)	2 / 7 (28.57%)
occurrences (all)	11	8	4
Vomiting			
subjects affected / exposed	4 / 53 (7.55%)	7 / 27 (25.93%)	3 / 7 (42.86%)
occurrences (all)	7	7	3
Abdominal pain			
subjects affected / exposed	4 / 53 (7.55%)	6 / 27 (22.22%)	2 / 7 (28.57%)
occurrences (all)	7	7	3
Dyspepsia			
subjects affected / exposed	4 / 53 (7.55%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	4	1	0
Abdominal distension			
subjects affected / exposed	3 / 53 (5.66%)	2 / 27 (7.41%)	1 / 7 (14.29%)
occurrences (all)	4	2	1
Dysphagia			

subjects affected / exposed	3 / 53 (5.66%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 53 (1.89%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Colitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	2 / 53 (3.77%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	3	2	0
Abdominal tenderness			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hepatomegaly			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Hyperbilirubinaemia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	6 / 53 (11.32%)	10 / 27 (37.04%)	1 / 7 (14.29%)
occurrences (all)	13	22	1
Night sweats			
subjects affected / exposed	3 / 53 (5.66%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Rash			
subjects affected / exposed	1 / 53 (1.89%)	5 / 27 (18.52%)	1 / 7 (14.29%)
occurrences (all)	1	11	1
Rash maculo-papular			
subjects affected / exposed	1 / 53 (1.89%)	4 / 27 (14.81%)	0 / 7 (0.00%)
occurrences (all)	1	5	0
Dry skin			
subjects affected / exposed	1 / 53 (1.89%)	3 / 27 (11.11%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Erythema ab igne			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Photosensitivity reaction			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Drug eruption			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	3 / 53 (5.66%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	3	2	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	3 / 53 (5.66%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Hyperthyroidism			
subjects affected / exposed	0 / 53 (0.00%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Empty sella syndrome			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 53 (18.87%)	4 / 27 (14.81%)	1 / 7 (14.29%)
occurrences (all)	10	4	2
Arthralgia			
subjects affected / exposed	8 / 53 (15.09%)	3 / 27 (11.11%)	2 / 7 (28.57%)
occurrences (all)	10	3	2
Pain in extremity			
subjects affected / exposed	6 / 53 (11.32%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	8	4	0
Myalgia			
subjects affected / exposed	5 / 53 (9.43%)	3 / 27 (11.11%)	1 / 7 (14.29%)
occurrences (all)	6	4	1
Muscular weakness			
subjects affected / exposed	3 / 53 (5.66%)	3 / 27 (11.11%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Musculoskeletal pain			
subjects affected / exposed	3 / 53 (5.66%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	3	2	0
Neck pain			
subjects affected / exposed	3 / 53 (5.66%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	3	2	0
Musculoskeletal chest pain			

subjects affected / exposed	2 / 53 (3.77%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	1 / 53 (1.89%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	4	1	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 53 (5.66%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	4	2	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 53 (5.66%)	4 / 27 (14.81%)	0 / 7 (0.00%)
occurrences (all)	3	5	0
Nasopharyngitis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Pneumonia			
subjects affected / exposed	1 / 53 (1.89%)	0 / 27 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
Candida infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Respiratory tract infection viral			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Genital candidiasis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Mastoiditis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Petrositis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pyelonephritis acute			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vestibular neuronitis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	2 / 53 (3.77%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	15 / 53 (28.30%)	8 / 27 (29.63%)	1 / 7 (14.29%)
occurrences (all)	19	8	3
Hyponatraemia			
subjects affected / exposed	6 / 53 (11.32%)	2 / 27 (7.41%)	0 / 7 (0.00%)
occurrences (all)	8	2	0
Dehydration			
subjects affected / exposed	4 / 53 (7.55%)	3 / 27 (11.11%)	1 / 7 (14.29%)
occurrences (all)	4	4	1
Hypoalbuminaemia			
subjects affected / exposed	5 / 53 (9.43%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	5	1	0
Hypokalaemia			
subjects affected / exposed	5 / 53 (9.43%)	3 / 27 (11.11%)	0 / 7 (0.00%)
occurrences (all)	8	6	0
Hypercalcaemia			

subjects affected / exposed	3 / 53 (5.66%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	3	2	0
Hypomagnesaemia			
subjects affected / exposed	2 / 53 (3.77%)	4 / 27 (14.81%)	0 / 7 (0.00%)
occurrences (all)	4	6	0
Cachexia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	2 / 53 (3.77%)	0 / 27 (0.00%)	1 / 7 (14.29%)
occurrences (all)	3	0	2
Hyperglycaemia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Hyperkalaemia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 27 (3.70%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Increased appetite			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tumour lysis syndrome			
subjects affected / exposed	0 / 53 (0.00%)	0 / 27 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Safety Population-Part C	Safety Population-Part D	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	94 / 98 (95.92%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	5	
Infected neoplasm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Skin papilloma			

subjects affected / exposed	2 / 11 (18.18%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Metastases to meninges			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Papilloma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	8 / 98 (8.16%)	
occurrences (all)	0	10	
Lymphostasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 11 (27.27%)	33 / 98 (33.67%)	
occurrences (all)	7	45	
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	11 / 98 (11.22%)	
occurrences (all)	1	12	
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	3	
Non-cardiac chest pain			
subjects affected / exposed	0 / 11 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	3	
Oedema peripheral			

subjects affected / exposed	1 / 11 (9.09%)	9 / 98 (9.18%)	
occurrences (all)	1	11	
Malaise			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	6	
Localised oedema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	0 / 11 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	5	
Peripheral swelling			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Chest pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Vaginal discharge			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 11 (9.09%)	16 / 98 (16.33%)	
occurrences (all)	1	18	
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	15 / 98 (15.31%)	
occurrences (all)	0	18	
Epistaxis			

subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Productive cough			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	3	
Haemoptysis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	4 / 98 (4.08%)	
occurrences (all)	0	5	
Depression			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 11 (18.18%)	9 / 98 (9.18%)	
occurrences (all)	2	11	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	14 / 98 (14.29%)	
occurrences (all)	1	15	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 11 (18.18%)	23 / 98 (23.47%)	
occurrences (all)	2	35	
Amylase increased			

subjects affected / exposed	2 / 11 (18.18%)	6 / 98 (6.12%)	
occurrences (all)	2	9	
Blood creatinine increased			
subjects affected / exposed	1 / 11 (9.09%)	10 / 98 (10.20%)	
occurrences (all)	1	20	
Lipase increased			
subjects affected / exposed	4 / 11 (36.36%)	8 / 98 (8.16%)	
occurrences (all)	9	13	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	3	
Blood bilirubin increased			
subjects affected / exposed	5 / 11 (45.45%)	1 / 98 (1.02%)	
occurrences (all)	10	1	
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Transaminases increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Body temperature increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Heart rate increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Protein total decreased			

subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	2 / 11 (18.18%)	12 / 98 (12.24%)	
occurrences (all)	2	18	
Blood albumin decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	4 / 11 (36.36%)	6 / 98 (6.12%)	
occurrences (all)	14	13	
Ligament sprain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Skin laceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Poisoning			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Sunburn			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)	12 / 98 (12.24%)	
occurrences (all)	0	13	
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	6	
Neuropathy peripheral			

subjects affected / exposed	0 / 11 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	4	
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	3	
Autonomic nervous system imbalance			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Complex regional pain syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Facial paresis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Taste disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vascular encephalopathy			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 11 (45.45%)	24 / 98 (24.49%)	
occurrences (all)	9	40	
Lymph node pain			
subjects affected / exposed	2 / 11 (18.18%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Neutropenia			

subjects affected / exposed	2 / 11 (18.18%)	2 / 98 (2.04%)	
occurrences (all)	6	5	
Blood loss anaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Eosinophilia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 98 (2.04%)	
occurrences (all)	1	6	
Lymph node haemorrhage			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	4	0	
Lymphocytosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Lymphopenia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Deafness neurosensory			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Keratitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 98 (1.02%)	
occurrences (all)	1	5	
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	0 / 11 (0.00%)	22 / 98 (22.45%)	
occurrences (all)	0	28	
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	14 / 98 (14.29%)	
occurrences (all)	0	17	
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	26 / 98 (26.53%)	
occurrences (all)	2	38	
Vomiting			
subjects affected / exposed	2 / 11 (18.18%)	17 / 98 (17.35%)	
occurrences (all)	4	22	
Abdominal pain			
subjects affected / exposed	1 / 11 (9.09%)	7 / 98 (7.14%)	
occurrences (all)	1	9	
Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Abdominal distension			
subjects affected / exposed	0 / 11 (0.00%)	4 / 98 (4.08%)	
occurrences (all)	0	4	
Dysphagia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	8 / 98 (8.16%)	
occurrences (all)	0	9	
Colitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	4 / 98 (4.08%)	
occurrences (all)	0	5	
Abdominal tenderness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	

Haemorrhoids			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Abdominal pain lower			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Oral pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	1 / 11 (9.09%)	5 / 98 (5.10%)	
occurrences (all)	1	5	
Abdominal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Hepatomegaly			
subjects affected / exposed	1 / 11 (9.09%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 11 (27.27%)	7 / 98 (7.14%)	
occurrences (all)	3	7	
Night sweats			
subjects affected / exposed	0 / 11 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	3	
Rash			
subjects affected / exposed	7 / 11 (63.64%)	14 / 98 (14.29%)	
occurrences (all)	14	18	
Rash maculo-papular			

subjects affected / exposed	1 / 11 (9.09%)	3 / 98 (3.06%)	
occurrences (all)	2	6	
Dry skin			
subjects affected / exposed	3 / 11 (27.27%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Erythema ab igne			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Photosensitivity reaction			
subjects affected / exposed	3 / 11 (27.27%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Alopecia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Drug eruption			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Hyperkeratosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 11 (9.09%)	4 / 98 (4.08%)	
occurrences (all)	1	4	
Hyperthyroidism			
subjects affected / exposed	0 / 11 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Empty sella syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 11 (0.00%)	11 / 98 (11.22%)	
occurrences (all)	0	13	
Arthralgia			
subjects affected / exposed	3 / 11 (27.27%)	12 / 98 (12.24%)	
occurrences (all)	6	15	
Pain in extremity			
subjects affected / exposed	0 / 11 (0.00%)	4 / 98 (4.08%)	
occurrences (all)	0	9	
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	8 / 98 (8.16%)	
occurrences (all)	0	12	
Muscular weakness			
subjects affected / exposed	0 / 11 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	5	
Musculoskeletal pain			
subjects affected / exposed	0 / 11 (0.00%)	8 / 98 (8.16%)	
occurrences (all)	0	9	
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	7	
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	5	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	11 / 98 (11.22%)	
occurrences (all)	0	12	
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	10 / 98 (10.20%)	
occurrences (all)	0	16	
Nasopharyngitis			

subjects affected / exposed	1 / 11 (9.09%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	8	
Candida infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Respiratory tract infection viral			
subjects affected / exposed	2 / 11 (18.18%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Conjunctivitis bacterial			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Ear infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Genital candidiasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Mastoiditis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Petrositis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis acute			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Vestibular neuronitis			

subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 11 (36.36%)	23 / 98 (23.47%)	
occurrences (all)	5	25	
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	7 / 98 (7.14%)	
occurrences (all)	0	9	
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	7	
Hypoalbuminaemia			
subjects affected / exposed	1 / 11 (9.09%)	7 / 98 (7.14%)	
occurrences (all)	1	7	
Hypokalaemia			
subjects affected / exposed	1 / 11 (9.09%)	3 / 98 (3.06%)	
occurrences (all)	1	4	
Hypercalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	5 / 98 (5.10%)	
occurrences (all)	0	5	
Hypomagnesaemia			
subjects affected / exposed	0 / 11 (0.00%)	6 / 98 (6.12%)	
occurrences (all)	0	8	
Cachexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 98 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	1 / 11 (9.09%)	6 / 98 (6.12%)	
occurrences (all)	1	10	

Hyperkalaemia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Increased appetite			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Tumour lysis syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 98 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2016	Module Amendment 1 (Global) (30 August 2016). For Part B1 of the trial, an additional dosing cohort was added, lowering the initial dose for CX-072 to 0.3 mg/kg. The 30 mg/kg CX-072 dosage was changed from an IV infusion duration of over 1 hour to ≥ 90 minutes. The Part B2 population for enrollment text was modified to remove patients with Hodgkin lymphoma with measurable disease. The Part C population for enrollment text was modified to include nonmeasurable BRAF V600E mutation–positive advanced melanoma. The Part D population for enrollment text was modified to clarify the diseases indicated must be measurable. Screening laboratory values were updated to clarify criteria for patients with HCC or pancreatic cancer for AST, ALT, and bilirubin, and to include criteria for amylase and lipase. An exclusion criterion was added for CAR T-cell containing regimens and AMD. Dose proportionality analysis was added. Reticulocyte counts were removed from the hematology assessment. Follow-up procedures for addressing events were added.
14 November 2016	Module Amendment 2 (Global) (14 November 2016) • The primary objective was modified to determine the maximum tolerated dose (MTD) and dose-limiting toxicities (DLTs) of CX-072 as monotherapy and in combination in predefined patient populations. • The secondary objectives were expanded to obtain preliminary evidence of anticancer activity on the basis of objective responses in patients treated with CX-072 as monotherapy in advanced or metastatic gastric and gastroesophageal junction (GEJ) tumors. • The study design was modified. • The DLT definitions were updated such that any Grade 5 adverse event, Grade 4 endocrinopathy, and Grade 2 pneumonitis or ocular toxicity necessitating discontinuation of CX-072 were designated as DLTs; the provision to exempt any Grade 3 toxicities (including immune-related) that resolve within 7 days as a DLT was removed; and Grade 3 adverse events of nausea, diarrhea, asthenia, constipation, pyrexia, and vomiting that resolve within 48 hours with appropriate treatment were specified as not considered a DLT. • The DLT evaluation period was increased from 21 days to 28 days for Parts A, B1, B2, and C. • A section was added specifying late stopping rules to be applied when ≥ 2 patients experience Grade ≥ 4 CX072–related adverse events beyond the DLT evaluation period. • A Safety Review Committee was added to monitor adverse event data and to provide recommendations related to dose escalation for the subsequent cohort. • The sample size was reduced for the study from approximately 300 patients to ≤ 149 patients and include further justification for the planned sample size. • The inclusion and exclusion criteria were modified to reflect the patient eligibility requirements specified in the updated study design; to remove barrier method as a highly effective method of contraception; and to exclude patients with prior history of myocarditis and prohibit the use of cytochrome P450 1A2 (CYP1A2) substrates, rather than CYP1B1 substrates.

19 January 2017	Module Amendment 3 (Global) (19 January 2017) • Nonclinical safety data were updated. • Secondary objectives were updated. • The length of treatment cycles was added for Parts A, B1, B2, C, and D. • Part B2 treatment regimen was updated from 3 doses to 4 doses of CX-072. • Language was added to indicate that a maximum of 4 doses of ipilimumab may be administered in Part B2. • The laboratory values for white blood cells, aspartate aminotransferase for patients in Part C, and total bilirubin in inclusion criterion 8 were updated. • Contraception requirements were updated to include acceptable contraceptive methods. • Exclusion criteria 2 and 14 were updated. • Guidelines for the management of allergic reactions were updated. • Statistical analysis of pharmacokinetic (PK) assessments was updated. • Details of the immunogenicity assessments were updated. • Biopsy collection in Parts B1 and B2 was clarified. • Optional serial collection of blood samples for measurement of exploratory biomarker for patients in Parts A, B1, and D was included. • The definition of adverse event was clarified. • Monitoring of adverse event data was updated to include the completion of an electronic serious adverse event (SAE) form for SAEs and added that the type of follow-up visit will be left to the discretion of the Investigator. • SAE reporting requirements were updated to include SAEs up to and including 30 days after administration of last dose of study drug and to include additional reporting instructions. • Reporting criteria of suspected and unexpected suspected adverse events were updated to include instructions for reporting to the Food and Drug Administration and applicable competent authorities in the European Union Member States concerned, and the Central Institutional Review Board/Ethics Committee.
13 July 2017	Module Amendment 4 (Global) (13 July 2017) • A cohort (Part A2) was added to the study to refine the selection of the MTD/maximum achieved dose. • The use of prior immunotherapies was clarified. • An additional exploratory objective was added to examine the relationship between dose/exposure and pharmacodynamics, safety, and efficacy for CX-072 monotherapy. • The late stopping rules were updated. • The patient’s tumor type in Part D was modified to undifferentiated pleomorphic sarcoma. • The sample size and statistical analyses was updated. • The inclusion/exclusion criteria were updated. • The packaging requirements and administration timing for vemurafenib was updated. • The management of allergic reactions was clarified. • A prior/concomitant medication exception was added allowing patients with prostate cancer to receive androgen deprivation therapy.

18 April 2018	Module Amendment 5 (Global) (18 April 2018). • The secondary and exploratory objectives were updated. • The 30 mg/kg dose of CX-072 was removed from Parts B1 and B2. • A 6 mg/kg dose of ipilimumab was added. • Language was added to indicated that a monotherapy dose expansion imaging substudy was to be performed in the Netherlands. • Tumor types in Part D were modified to include small bowel adenocarcinoma, cutaneous squamous cell carcinoma, Merkel cell carcinoma, thymic carcinoma, anal squamous cell carcinoma, triple-negative breast cancer, and high tumor mutational burden. • The language to allow for cohort over enrollment so enough evaluable patients for DLT evaluation was removed. • The sample size and statistical analyses were updated to reflect changes to CX-072 dose, ipilimumab dose, and Part D tumor type additions. • The inclusion and exclusion criteria were updated. • The use of concomitant medications for patients with triple-negative breast cancer was specified. • A blood sample for tumor mutation burden (Part D) and blood sample for thymoma safety monitoring (Parts A and A2) was added. • The exact dose for each infusion was specified to be calculated based on the patient's body weight from the specific dosing visit. • A 3-hour postdose (vemurafenib) PK sample on Cycle 1 Day 1 was added for Part C. • Adverse event language was clarified. • Appendix 2 was added to include information on thymic carcinoma classification and staging.
02 November 2018	Module Amendment 6 (Global) (02 November 2018) • The introduction and study rationale for dose escalation and dose expansion was updated. • Part E (Response Evaluation of CX-072 Monotherapy with Fixed Dosing) was added because encouraging safety and antitumor activity was observed in patients treated with at least 1 dose of CX-072 monotherapy at ≥ 3 mg/kg. These data warranted planning for confirming antitumor activity that might be observed in Part D by implementing an appropriately designed Part E with clear criteria for advancement from Part D to Part E, based on objective response rates. • The language of the primary, secondary, and exploratory objectives was updated for Parts A to D and defined for Part E. • The 10 mg/kg ipilimumab dose was removed from Parts B1 and B2 due to the increased toxicity according to published ipilimumab safety data. • Intra-patient dose escalation was added for patients in Cohorts 3A2, 4A2, and 5A2. • Language was added to discourage further enrollment of patients in Part B2 receiving CX-072 run-in phased dosing of CX-072 in combination with ipilimumab. Future patients enrolling in Part B2 were to receive CX072 administered in a concomitant combination schedule with ipilimumab. • Language was updated to clarify that TET encompasses thymic epithelial tumors, which includes thymoma and thymic carcinoma. • Assessment of dose-limiting toxicities was clarified for vemurafenib. • The sample size determination and statistical analyses was updated to reflect the addition of Part E and define the criteria for cohort expansion in Part D and assumptions and criteria for Simon's 2-stage design in Part E. • The inclusion criteria were updated to clarify Part D criteria and define Part E criteria to limit prior lines of therapy to target patient populations that are more likely to benefit from participation in the trial. • Inclusion criterion 8 was updated to define acceptable contraception methods and introduce Appendix 5.
20 February 2020	Module Amendment 7 (Global) (03 April 2020) Not Submitted
04 June 2020	Module Amendment 8 (Global) (04 June 2020) Updates were made to reflect the addition of a long-term extension to the study.

19 August 2020	Module Amendment 9 (Global) (19 August 2020) Updates were made to reflect the commitments made to the UK MHRA for changes to the long-term extension study safety assessment and to clarify the purpose of the long-term extension study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34253583

http://www.ncbi.nlm.nih.gov/pubmed/34301809

http://www.ncbi.nlm.nih.gov/pubmed/34301808

http://www.ncbi.nlm.nih.gov/pubmed/32681519