



Clinical trial results:

A Modular, Multi-part, Multi-arm, Open-label, Phase I/IIa Study to Evaluate the Safety and Tolerability of CT7001 Alone and in Combination with Anti-cancer Treatments in Patients with Advanced Malignancies

Summary

EudraCT number	2017-002026-20
Trial protocol	GB
Global end of trial date	15 December 2022

Results information

Result version number	v1 (current)
This version publication date	31 March 2024
First version publication date	31 March 2024

Trial information

Trial identification

Sponsor protocol code	CT7001-001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03363893
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Carrick Therapeutics Limited
Sponsor organisation address	Regus Dublin Blanchardstown Block 1, Blanchardstown Corporate Park Ballycoolin Road Blanchardstown, Dublin, Ireland, 15 D15 AKK1
Public contact	Sheila O Mahony, Carrick Therapeutics Limited, +353 1 5996873, trials@carricktherapeutics.com
Scientific contact	Sheila O Mahony, Carrick Therapeutics Limited, +353 1 5996873, trials@carricktherapeutics.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	15 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 December 2022
Global end of trial reached?	Yes
Global end of trial date	15 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Core: To investigate the safety and tolerability of CT7001 given alone or in combination with anticancer treatments

Module 1A: To select the CT7001 dose(s) and schedule(s) for further clinical evaluation in patients with advanced solid malignancies.

Module 1B-1: To further characterize the safety and tolerability of CT7001 and determine the most appropriate

dosing regimen for subsequent Phase 2 testing (definitive recommended Phase 2 dose).

Module 1B-2: To assess the biological and anti-tumor activity of CT7001, given as a monotherapy.

Module 2A: To determine the recommended Phase 2 dose (RP2D) of CT7001 given in combination with fulvestrant at 500 mg.

Module 4: To evaluate the effect of food on the total and peak exposure of CT7001 when dosed as a capsule formulation to patients with advanced solid malignancies

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki and in compliance with the National Health Service Research Governance Framework, International Council for Harmonization (ICH) Good Clinical Practice (GCP(CPMP/ICH/135/95, Jul 1996) and subsequent R2 amendment, the European Directive on Clinical Trials (2001/20/EC, 04 Apr 2001 and subsequent amendments) and the European Directive on GCP (2005/28/EC).

All subjects were provided written informed consent before undergoing any trial related procedures. Safety of the subjects was safeguarded through safety data review and the implementation of study stopping criteria.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 111
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	124
EEA total number of subjects	0

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)	79
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study recruited participants at least 18 years of age with histological or cytological confirmation of an advanced malignancy, with an Eastern Cooperative Oncology Group (ECOG) status of 0 or 1 and an estimated life expectancy greater than 12 weeks.

25 sites in total, 11 sites in the UK and 14 sites in the US participated in the study.

Pre-assignment

Screening details:

A total of 174 participants were recruited, of which 124 participants were enrolled and went on to receive study treatment with CT7001. Of the 174 participants screened, 50 participants did not receive study treatment, of which 46 participants did not meet the study enrolment criteria and 4 participants withdrew from the study.

Pre-assignment period milestones

Number of subjects started	174 ^[1]
Number of subjects completed	124

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 4
Reason: Number of subjects	Screening failure: 46

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 174 participants were recruited, of which 124 participants were enrolled and went on to receive study treatment with CT7001. Of the 174 participants screened, 50 participants did not receive study treatment, of which 46 participants did not meet the study enrolment criteria and 4 participants withdrew from the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Module 1 Part A-Cohort 1 120mg OD

Arm description:

Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CT7001 capsules orally were taken as a single dose (120 mg for Cohort 1) on Cycle 0 Day 1 with a minimum of a 48-hour washout period following this dose.

Cycle 1 dosing then began as a once daily dosing regimen on Cycle 1 Day 1 (C1D1). A cycle of study treatment (after Cycle 0) was for a minimum of 21 days.

Arm title	Module 1 Part A-Cohort 2 240 mg OD
<p>Arm description:</p> <p>Dose Escalation Phase-Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose</p>	
Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
<p>Dosage and administration details:</p> <p>CT7001 capsules orally were taken as a single dose (240 mg for Cohort 2) on Cycle 0 Day 1 with a minimum of a 48-hour washout period following this dose.</p> <p>Cycle 1 dosing then began as a once daily dosing regimen on Cycle 1 Day 1 (C1D1). A cycle of study treatment (after Cycle 0) was for a minimum of 21 days.</p>	
Arm title	Module 1 Part A-Cohort 3 480 mg OD
<p>Arm description:</p> <p>Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.</p>	
Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
<p>Dosage and administration details:</p> <p>CT7001 capsules orally were taken as a single dose (480 mg for Cohort 3) on Cycle 0 Day 1 with a minimum of a 48-hour washout period following this dose.</p> <p>Cycle 1 dosing then began as a once daily dosing regimen on Cycle 1 Day 1 (C1D1). A cycle of study treatment (after Cycle 0) was for a minimum of 21 days.</p>	
Arm title	Module 1 Part A-Cohort 4 360 mg OD
<p>Arm description:</p> <p>Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose.</p>	
Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
<p>Dosage and administration details:</p> <p>CT7001 capsules orally were taken as a single dose (360 mg for Cohort 4) on Cycle 0 Day 1 with a minimum of a 48-hour washout period following this dose.</p> <p>Cycle 1 dosing then began as a once daily dosing regimen on Cycle 1 Day 1 (C1D1). A cycle of study treatment (after Cycle 0) was for a minimum of 21 days.</p>	
Arm title	Module 1 Part A-Cohort 5 180 mg BID

Arm description:

Dose Escalation Phase-Participants received twice daily dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CT7001 capsules orally were taken as 180 mg twice daily (for Cohort 5) on Cycle 0 Day 1 with a minimum of a 48-hour washout period following this dose.

Cycle 1 dosing then began as twice daily dosing regimen on Cycle 1 Day 1 (C1D1). A cycle of study treatment (after Cycle 0) was for a minimum of 21 days.

Arm title	Module 1 Part B-1 360mg OD (TNBC)
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Arm description:

In this Module 1B-1, CT7001 was administered to participants with advanced TNBC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).

Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CT7001 capsules orally were taken as 360 mg once daily.

Arm title	Module 1 Part B-2 360mg OD (CRPC)
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Arm description:

In this Module 1B-2, CT7001 was administered to participants with advanced CRPC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).

Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CT7001 capsules orally were taken as 360 mg once daily.

Arm title	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)
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Arm description:

Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C.

In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 1 tested CT7001 at 240 mg once daily (OD), which is approximately 33% lower than the preliminary RP2D as monotherapy (360 mg).

Arm type	Experimental
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Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
CT7001 capsules orally in either a fed or fasted state were taken as 240 mg once daily (OD).	
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Fulvestrant 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose, administered as 2 consecutive slow intramuscular injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area).	
Arm title	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)
Arm description:	
Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C. In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 2 tested CT7001 at 360 mg once daily (OD).	
Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
CT7001 capsules orally in either a fed or fasted state were taken as 360 mg once daily.	
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Fulvestrant 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose, administered as 2 consecutive slow intramuscular injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area).	
Arm title	Module 4-120 mg OD
Arm description:	
Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase. Sequence 1: 120 mg CT7001 fed in Period 1 followed by 120 mg CT7001 fasted in Period 2. Sequence 2: 120 mg CT7001 fasted in Period 1 followed by 120 mg CT7001 fed in Period 2.	
Arm type	Experimental

Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CT7001 Capsules orally, 120 mg fed in Period 1 followed by 120 mg CT7001 fasted in Period 2, followed by 240 mg once daily (OD) in the continuous dosing phase.

Arm title	Module 4 360 mg OD
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Arm description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 3: 360 mg CT7001 fed in Period 1 followed by 360 mg CT7001 fasted in Period 2.

Sequence 4: 360 mg CT7001 fasted in Period 1 followed by 360 mg CT7001 fed in Period 2.

Arm type	Experimental
Investigational medicinal product name	CT7001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

CT7001 capsules orally, 360 mg fed in Period 1 followed by 360 mg CT7001 fasted in Period 2, followed by 360 mg once daily (OD) in the continuous dosing phase.

Number of subjects in period 1	Module 1 Part A-Cohort 1 120mg OD	Module 1 Part A-Cohort 2 240 mg OD	Module 1 Part A-Cohort 3 480 mg OD
Started	6	12	6
Completed	6	12	6

Number of subjects in period 1	Module 1 Part A-Cohort 4 360 mg OD	Module 1 Part A-Cohort 5 180 mg BID	Module 1 Part B-1 360mg OD (TNBC)
Started	12	8	23
Completed	12	8	23

Number of subjects in period 1	Module 1 Part B-2 360mg OD (CRPC)	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)
Started	11	6	25
Completed	11	6	25

Number of subjects in period 1	Module 4-120 mg OD	Module 4 360 mg OD
Started	8	7
Completed	8	7

Baseline characteristics

Reporting groups

Reporting group title	Module 1 Part A-Cohort 1 120mg OD
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Reporting group description:

Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Reporting group title	Module 1 Part A-Cohort 2 240 mg OD
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Reporting group description:

Dose Escalation Phase-Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose

Reporting group title	Module 1 Part A-Cohort 3 480 mg OD
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Reporting group description:

Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Reporting group title	Module 1 Part A-Cohort 4 360 mg OD
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Reporting group description:

Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose.

Reporting group title	Module 1 Part A-Cohort 5 180 mg BID
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Reporting group description:

Dose Escalation Phase-Participants received twice daily dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Reporting group title	Module 1 Part B-1 360mg OD (TNBC)
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Reporting group description:

In this Module 1B-1, CT7001 was administered to participants with advanced TNBC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).

Reporting group title	Module 1 Part B-2 360mg OD (CRPC)
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Reporting group description:

In this Module 1B-2, CT7001 was administered to participants with advanced CRPC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).

Reporting group title	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)
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Reporting group description:

Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C.

In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 1 tested CT7001 at 240 mg once daily (OD), which is approximately 33% lower than the preliminary RP2D as monotherapy (360 mg).

Reporting group title	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)
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Reporting group description:

Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C.

In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 2 tested CT7001 at 360 mg once daily (OD).

Reporting group title	Module 4-120 mg OD
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Reporting group description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 1: 120 mg CT7001 fed in Period 1 followed by 120 mg CT7001 fasted in Period 2.

Sequence 2: 120 mg CT7001 fasted in Period 1 followed by 120 mg CT7001 fed in Period 2.

Reporting group title	Module 4 360 mg OD
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Reporting group description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 3: 360 mg CT7001 fed in Period 1 followed by 360 mg CT7001 fasted in Period 2.

Sequence 4: 360 mg CT7001 fasted in Period 1 followed by 360 mg CT7001 fed in Period 2.

Reporting group values	Module 1 Part A-Cohort 1 120mg OD	Module 1 Part A-Cohort 2 240 mg OD	Module 1 Part A-Cohort 3 480 mg OD
Number of subjects	6	12	6
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	7	6
From 65-84 years	1	5	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	4	7	6
Male	2	5	0

Reporting group values	Module 1 Part A-Cohort 4 360 mg OD	Module 1 Part A-Cohort 5 180 mg BID	Module 1 Part B-1 360mg OD (TNBC)
Number of subjects	12	8	23
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0

Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	4	19
From 65-84 years	5	4	4
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	9	6	23
Male	3	2	0

Reporting group values	Module 1 Part B-2 360mg OD (CRPC)	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)
Number of subjects	11	6	25
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	5	15
From 65-84 years	6	1	10
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	6	25
Male	11	0	0

Reporting group values	Module 4-120 mg OD	Module 4 360 mg OD	Total
Number of subjects	8	7	124
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	79
From 65-84 years	5	4	45
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	2	3	91
Male	6	4	33

End points

End points reporting groups

Reporting group title	Module 1 Part A-Cohort 1 120mg OD
Reporting group description: Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.	
Reporting group title	Module 1 Part A-Cohort 2 240 mg OD
Reporting group description: Dose Escalation Phase-Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose	
Reporting group title	Module 1 Part A-Cohort 3 480 mg OD
Reporting group description: Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.	
Reporting group title	Module 1 Part A-Cohort 4 360 mg OD
Reporting group description: Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose.	
Reporting group title	Module 1 Part A-Cohort 5 180 mg BID
Reporting group description: Dose Escalation Phase-Participants received twice daily dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.	
Reporting group title	Module 1 Part B-1 360mg OD (TNBC)
Reporting group description: In this Module 1B-1, CT7001 was administered to participants with advanced TNBC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).	
Reporting group title	Module 1 Part B-2 360mg OD (CRPC)
Reporting group description: In this Module 1B-2, CT7001 was administered to participants with advanced CRPC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).	
Reporting group title	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)
Reporting group description: Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C. In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 1 tested CT7001 at 240 mg once daily (OD), which is approximately 33% lower than the preliminary RP2D as monotherapy (360 mg).	
Reporting group title	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)

Reporting group description:

Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C.

In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 \pm 2 days with an additional 500 mg dose given 14 \pm 2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 2 tested CT7001 at 360 mg once daily (OD).

Reporting group title	Module 4-120 mg OD
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Reporting group description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 1: 120 mg CT7001 fed in Period 1 followed by 120 mg CT7001 fasted in Period 2.

Sequence 2: 120 mg CT7001 fasted in Period 1 followed by 120 mg CT7001 fed in Period 2.

Reporting group title	Module 4 360 mg OD
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Reporting group description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 3: 360 mg CT7001 fed in Period 1 followed by 360 mg CT7001 fasted in Period 2.

Sequence 4: 360 mg CT7001 fasted in Period 1 followed by 360 mg CT7001 fed in Period 2.

Subject analysis set title	Module 4-120 mg OD Fed - fasted (Sequence 1)
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Subject analysis set type	Per protocol
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Subject analysis set description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 1: 120 mg CT7001 fed in Period 1 followed by 120 mg CT7001 fasted in Period 2.

Subject analysis set title	Module 4 120 mg OD Fasted-Fed (Sequence 2)
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Subject analysis set type	Per protocol
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Subject analysis set description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 2: 120 mg CT7001 fasted in Period 1 followed by 120 mg CT7001 fed in Period 2

Subject analysis set title	Module 4 360 mg OD Fed - fasted (Sequence 3)
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Subject analysis set type	Per protocol
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Subject analysis set description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 3: 360 mg CT7001 fed in Period 1 followed by 360 mg CT7001 fasted in Period 2.

Subject analysis set title	Module 4 360 mg OD Fasted- fed (Sequence 4)
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Subject analysis set type	Per protocol
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Subject analysis set description:

Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.

Sequence 4: 360 mg CT7001 fasted in Period 1 followed by 360 mg CT7001 fed in Period 2.

Primary: Number of participants with one or more Treatment Emergent Adverse Events (TEAEs)

End point title	Number of participants with one or more Treatment Emergent Adverse Events (TEAEs) ^[1]
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End point description:

Adverse events were recorded for each participant with causality (relationship or otherwise to study treatment) assessed by investigator. Treatment-emergent adverse events (TEAEs) are defined as those AEs which occur from Cycle 0 Day 1/Cycle 1 Day 1 of the study module to 28 days after the last dose of CT7001 in a module. Adverse events termed "related" are those assessed by the investigator as possibly

related, probably related, or related to CT7001.

End point type	Primary
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End point timeframe:

From first dose of study drug to participant (for non-serious AEs) or provision of informed consent (serious AEs [SAEs]) until the end of study visit (28 - 35 days after last dose of study drug).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical analysis were carried out. All data were summarized using standard summary statistics and were descriptive in nature.

End point values	Module 1 Part A-Cohort 1 120mg OD	Module 1 Part A-Cohort 2 240 mg OD	Module 1 Part A-Cohort 3 480 mg OD	Module 1 Part A-Cohort 4 360 mg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	6	12
Units: Participants				
Participants with one or more TEAE	6	12	6	12
Participants with one or more related TEAEs	6	12	6	12

End point values	Module 1 Part A-Cohort 5 180 mg BID	Module 1 Part B-1 360mg OD (TNBC)	Module 1 Part B-2 360mg OD (CRPC)	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	23	11	6 ^[2]
Units: Participants				
Participants with one or more TEAE	8	23	11	6
Participants with one or more related TEAEs	8	22	11	6

Notes:

[2] - AEs were assessed in relation to CT7001 and Fulvestrant. Data shown describes AEs related to CT7001.

End point values	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)	Module 4-120 mg OD	Module 4 360 mg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25 ^[3]	8 ^[4]	7 ^[5]	
Units: Participants				
Participants with one or more TEAE	25	8	7	
Participants with one or more related TEAEs	24	8	7	

Notes:

[3] - AEs were assessed in relation to CT7001 and Fulvestrant. Data shown describes AEs related to CT7001.

[4] - Results reported for the entire study period (crossover phase and continuous dosing phase combined)

[5] - Results reported for the entire study period (crossover phase and continuous dosing phase combined)

Statistical analyses

Primary: Number of participants with Serious adverse events (SAEs)

End point title	Number of participants with Serious adverse events (SAEs) ^[6]
End point description:	
Serious adverse events (SAEs) are defined as any untoward medical occurrence that results in death, hospitalisation or prolongation of existing hospitalisation, persistent or significant disability/incapacity or a congenital anomaly or birth defect. Adverse events are classed as "related" if the event was assessed by investigator as probably related, possibly related, or related to CT7001 treatment.	
End point type	Primary
End point timeframe:	
Provision of informed consent until 28 days after last dose of study drug	

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical analysis were carried out. All data were summarized using standard summary statistics and were descriptive in nature.

End point values	Module 1 Part A-Cohort 1 120mg OD	Module 1 Part A-Cohort 2 240 mg OD	Module 1 Part A-Cohort 3 480 mg OD	Module 1 Part A-Cohort 4 360 mg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	6	12
Units: Participants				
Number of participants experiencing SAE	1	4	1	3
Number of SAEs related to CT7001	0	0	0	0
Number of SAEs not related to CT7001	1	4	1	5

End point values	Module 1 Part A-Cohort 5 180 mg BID	Module 1 Part B-1 360mg OD (TNBC)	Module 1 Part B-2 360mg OD (CRPC)	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	23	11	6
Units: Participants				
Number of participants experiencing SAE	3	9	2	2
Number of SAEs related to CT7001	0	4	0	1
Number of SAEs not related to CT7001	3	15	2	1

End point values	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)	Module 4-120 mg OD	Module 4 360 mg OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	8 ^[7]	7 ^[8]	
Units: Participants				

Number of participants experiencing SAE	8	0	4	
Number of SAEs related to CT7001	1	0	1	
Number of SAEs not related to CT7001	7	0	4	

Notes:

[7] - Results reported for the entire study period (crossover phase and continuous dosing phase combined)

[8] - Results reported for the entire study period (crossover phase and continuous dosing phase combined)

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Grade 3 or higher AEs reported in >1 participant

End point title	Incidence of Grade 3 or higher AEs reported in >1 participant ^[9]
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End point description:

Adverse events (AEs) were collected throughout the study and assigned grades by the investigator: Grade 1 (mild AE), Grade 2 (moderate), Grade 3 (severe), Grade 4 (life threatening) or Grade 5 (fatal). This data describes the number of participants who experienced one or more AEs assessed as maximum Grade 3, 4 or 5.

End point type	Primary
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End point timeframe:

From first dose of study drug to participant (for non-serious AEs) or provision of informed consent (serious AEs [SAEs]) until the end of study visit (28 - 35 days after last dose of study drug).

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical analysis were carried out. All data were summarized using standard summary statistics and were descriptive in nature.

End point values	Module 1 Part A-Cohort 1 120mg OD	Module 1 Part A-Cohort 2 240 mg OD	Module 1 Part A-Cohort 3 480 mg OD	Module 1 Part A-Cohort 4 360 mg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	6	12
Units: Participants				
Participants with any Grade 3 or higher AE	2	6	4	6

End point values	Module 1 Part A-Cohort 5 180 mg BID	Module 1 Part B-1 360mg OD (TNBC)	Module 1 Part B-2 360mg OD (CRPC)	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	23	11	6
Units: Participants				
Participants with any Grade 3 or higher AE	3	10	11	4

End point values	Module 2 Part A CT7001 360	Module 4-120 mg OD	Module 4 360 mg OD	
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	mg OD + fulvestrant (Cohort 2)			
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	8 ^[10]	7 ^[11]	
Units: Participants				
Participants with any Grade 3 or higher AE	17	1	4	

Notes:

[10] - Results reported for the entire study period (crossover phase and continuous dosing phase combined)

[11] - Results reported for the entire study period (crossover phase and continuous dosing phase combined)

Statistical analyses

No statistical analyses for this end point

Primary: Best Objective Response (BOR) following study treatment (Module 1 Part B-2 only)

End point title	Best Objective Response (BOR) following study treatment (Module 1 Part B-2 only) ^{[12][13]}
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End point description:

At each tumor assessment visit, participants were assigned tumor responses of complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) by the investigator according to RECIST (Response Evaluation Criteria in Solid Tumours) V1.1. The best objective response (BOR) was determined for each participant based on the best response recorded from the start of study treatment to the end of treatment, including any assessments for confirmation after the end of treatment. CR defined as disappearance of all target lesions; PR as at least a 30% decrease in the sum of diameters of target lesions; PD as at least a 20% increase in the sum of diameters of target lesions; SD as neither sufficient shrinkage to qualify for PR, nor sufficient increase to qualify for PD.

End point type	Primary
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End point timeframe:

Start of study treatment to end of treatment (including any assessments for confirmation after the end of treatment)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical analysis were carried out. All data were summarized using standard summary statistics and were descriptive in nature.

[13] - 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: Results reported as this was the primary endpoint for Module 1 Part B-2 only based on the primary objective.

End point values	Module 1 Part B-2 360mg OD (CRPC)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Participants				
Complete response (CR)	0			
Partial response (PR)	0			
Stable disease (SD)	5			
Progressive disease (PD)	5			
Not evaluable	1			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum observed plasma concentration (Cmax) of CT7001 (Module 4 only)

End point title	Maximum observed plasma concentration (Cmax) of CT7001 (Module 4 only) ^[14]
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End point description:

Cmax is the maximum observed plasma concentration of CT7001 following oral dosing. The primary objective specific to Module 4 was to evaluate the effect of food on total and peak exposure of CT7001 when dosed as a capsule formulation to patients with advanced solid malignancies. Participants received either 120 mg (Cohort 1) or 360 mg (Cohort 2) of CT7001 as a single dose in the fed state in Period 1 and another single dose in the fed state in Period 2, or vice versa. The two doses were separated by a washout period of 7 days. After participants completed the single dose fed/fasted crossover phase, they continued into the continuous dosing phase of the module (Period 2 Day 8 of the crossover phase = Cycle 1 Day 1 of the continuous dosing phase) which continued until disease progression, death, prohibitive toxicity, or withdrawal of consent by participant.

End point type	Primary
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End point timeframe:

Pre-dose Cycle 0 Day 1 to 24 hours post-dose Cycle 2 Day 1 (before Cycle 2 Day 2 dose)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical analysis were carried out. All data were summarized using standard summary statistics and were descriptive in nature.

End point values	Module 4-120 mg OD Fed - fasted (Sequence 1)	Module 4 120 mg OD Fasted-Fed (Sequence 2)	Module 4 360 mg OD Fed - fasted (Sequence 3)	Module 4 360 mg OD Fasted-fed (Sequence 4)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	6	4
Units: ng/mL				
geometric mean (full range (min-max))				
Cmax	19.21 (3.41 to 53.1)	63.77 (14.4 to 238)	138.8 (113 to 195)	176.1 (52.6 to 302)

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve (AUC) 0-∞ (Module 4 only)

End point title	Area under the plasma concentration-time curve (AUC) 0-∞ (Module 4 only) ^[15]
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End point description:

Area under the plasma concentration-time curve from time 0 extrapolated to infinity (AUC 0-∞) was

used in the evaluation of the effect of food on the total and peak exposure of CT7001 (where AUC_{0-∞} could not be calculated, AUC 0-72 hours was used in the evaluation). Participants received either 120 mg (Cohort 1) or 360 mg (Cohort 2) of CT7001 as a single dose in the fed state in Period 1 and another single dose in the fed state in Period 2, or vice versa. The two doses were separated by a washout period of 7 days. After participants completed the single dose fed/fasted crossover phase, they continued into the continuous dosing phase of the module (Period 2 Day 8 of the crossover phase = Cycle 1 Day 1 of the continuous dosing phase) which continued until disease progression, death, prohibitive toxicity, or withdrawal of consent.

End point type	Primary
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End point timeframe:

Pre-dose to 168 hours following oral administration of single dose of CT7001

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical analysis were carried out. All data were summarized using standard summary statistics and were descriptive in nature.

End point values	Module 4-120 mg OD Fed - fasted (Sequence 1)	Module 4 120 mg OD Fasted-Fed (Sequence 2)	Module 4 360 mg OD Fed - fasted (Sequence 3)	Module 4 360 mg OD Fasted-fed (Sequence 4)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3 ^[16]	7 ^[17]	5 ^[18]	7
Units: h.ng/ml				
geometric mean (full range (min-max))	785.3 (719 to 925)	694.9 (294 to 1470)	2696 (1500 to 3710)	2545 (766 to 4760)

Notes:

[16] - Only 3 participants contributed to AUC_{0-∞} in fed state

[17] - Only 7 participants contributed to AUC_{0-∞} in fasted state

[18] - Only 5 participants contributed to AUC_{0-∞} in fed state

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs were continuously monitored throughout the study from signing of the ICF through to the end of study visit.

AEs (non-serious) were recorded from the time the participant had taken at least 1 dose of IMP through to the participant's last visit.

Adverse event reporting additional description:

AEs and TEAEs from all cycles of treatment were presented graphically, as deemed appropriate.

These were summarized by MedDRA system organ class (SOC), preferred term (PT), and Common Terminology Criteria for Adverse Events (CTCAE) grade. Serious adverse events (SAEs) were analyzed and reported separately.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Module 1 Part A-Cohort 1 120mg OD
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Reporting group description:

Dose Escalation Phase-Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Reporting group title	Module 1 Part A-Cohort 2 240 mg OD
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Reporting group description:

Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose.

Reporting group title	Module 1 Part A-Cohort 3 480 mg OD
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Reporting group description:

Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Reporting group title	Module 1 Part A-Cohort 4 360 mg OD
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Reporting group description:

Participants received a single dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted. Once the MBAD was determined and agreed by the SRC, the paired biopsy expansion cohort in patients with breast cancer commenced at the selected dose.

Reporting group title	Module 1 Part A-Cohort 5 180 mg BID
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Reporting group description:

Dose Escalation Phase-Participants received twice daily dose of CT7001 on Day 1 of Cycle 0 (C0D1) followed by a 2-day washout period (C0D2), before receiving cycles of 21 continuous days dosing of CT7001 capsules. Dosing was continued until the participant was no longer gaining clinical benefit or another treatment discontinuation criterion was met, at which time an end of treatment visit was conducted.

Reporting group title	Module 1 Part B-1 360mg OD (TNBC)
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Reporting group description:

In this Module 1B-1, CT7001 was administered to participants with advanced TNBC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).

Reporting group title	Module 1 Part B-2 360mg OD (CRPC)
Reporting group description:	
In this Module 1B-2, CT7001 was administered to participants with advanced CRPC at the maximum tolerated dose (MTD) identified from Module 1A (360 mg once daily [OD]).	
Reporting group title	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)
Reporting group description:	
Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C.	
In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 1 tested CT7001 at 240 mg once daily (OD), which is approximately 33% lower than the preliminary RP2D as monotherapy (360 mg).	
Reporting group title	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)
Reporting group description:	
Module 2 was to comprise of 3 parts (A, B and C). This study results summary details the results from Part A, an open-label, single-arm, ascending dose study to determine the dosing regimen of CT7001 and fulvestrant. Part A proved sufficient to inform the next studies to be conducted within the development program, therefore no further details are provided on Parts B and C.	
In each cohort, the dose of fulvestrant was fixed at the standard dose of 500 mg given at intervals of 28 ±2 days with an additional 500 mg dose given 14 ±2 days after the first dose. Fulvestrant was administered as 2 consecutive slow intramuscular (i.m.) injections (1-2 minutes) of 250 mg in 5 mL, one in each buttock (gluteal area). Cohort 2 tested CT7001 at 360 mg once daily (OD).	
Reporting group title	Module 4-120 mg OD
Reporting group description:	
Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.	
Participants treated with 120 mg CT7001 OD in this cohort.	
Reporting group title	Module 4 360 mg OD
Reporting group description:	
Module 4 evaluated the effect of food on the PK of CT7001 using a randomized, balanced, single-dose, two-treatment (fed vs. fasting), two-period, two-sequence crossover design, followed by a continuous treatment phase.	
Participants treated with 360 mg CT7001 OD in this cohort.	

Serious adverse events	Module 1 Part A- Cohort 1 120mg OD	Module 1 Part A- Cohort 2 240 mg OD	Module 1 Part A- Cohort 3 480 mg OD
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	4 / 12 (33.33%)	1 / 6 (16.67%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	0 / 6 (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
Metastases to central nervous system			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Disease progression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (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
Diaphragm muscle weakness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (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
Pulmonary embolism			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea at rest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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 graft occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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 flutter			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (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
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Appendicitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (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
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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 infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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			
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
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	Module 1 Part A-Cohort 4 360 mg OD	Module 1 Part A-Cohort 5 180 mg BID	Module 1 Part B-1 360mg OD (TNBC)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)	3 / 8 (37.50%)	9 / 23 (39.13%)
number of deaths (all causes)	0	0	2
number of deaths resulting from	0	0	2

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung neoplasm malignant			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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			
Disease progression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragm muscle weakness			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea at rest			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (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
Injury, poisoning and procedural			

complications			
Fall			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular graft occlusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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 flutter			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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			
Presyncope			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (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
Cerebral haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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			
Thrombocytopenia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	2 / 23 (8.70%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (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
Large intestine perforation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (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
Oesophagitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic hernia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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			
Appendicitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (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
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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			
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
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	Module 1 Part B-2 360mg OD (CRPC)	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	8 / 25 (32.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
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			
Hypotension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (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
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal			

disorders			
Lung disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragm muscle weakness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea at rest			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
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			
Fall			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
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 graft occlusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
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 flutter			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (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
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior reversible encephalopathy syndrome			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
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	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (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
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (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
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic hernia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (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
Liver injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
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 infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Upper respiratory tract infection subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (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
Atypical pneumonia subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (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
COVID-19 subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
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 pneumonia subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
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			
Hyperglycaemia subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Module 4-120 mg OD	Module 4 360 mg OD	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	4 / 7 (57.14%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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			
Lung disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragm muscle weakness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea at rest			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Oesophagitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	2 / 7 (28.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Parainfluenzae virus infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (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 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acidosis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Module 1 Part A-Cohort 1 120mg OD	Module 1 Part A-Cohort 2 240 mg OD	Module 1 Part A-Cohort 3 480 mg OD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	12 / 12 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breast cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypotension			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Chest tube insertion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tooth repair			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)	7 / 12 (58.33%)	0 / 6 (0.00%)
occurrences (all)	2	7	0
Crepitations			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Biliary tract infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Facial pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Reproductive system and breast disorders			
Menometrorrhagia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Breast pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breast discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nipple exudate bloody			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Priapism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	5 / 6 (83.33%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	5	1	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	4 / 12 (33.33%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
Dyspnoea			
subjects affected / exposed	2 / 6 (33.33%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	2	1	2
Pleural effusion			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea at rest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Emotional distress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Blood creatine increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	2 / 6 (33.33%)
occurrences (all)	2	1	3
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
White blood cell count decreased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymph node palpable			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood magnesium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Reticulocyte count increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Blood urea increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 12 (8.33%) 2	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Clavicle fracture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Multiple fractures subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Burn oral cavity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Thermal burn subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1
Sunburn			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Atrial flutter			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Neuralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Intention tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ageusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyskinesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electric shock sensation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lethargy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cluster headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	5 / 12 (41.67%)	1 / 6 (16.67%)
occurrences (all)	5	7	1
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Visual impairment			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye discharge			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 6 (100.00%)	8 / 12 (66.67%)	5 / 6 (83.33%)
occurrences (all)	10	11	15
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Vomiting			
subjects affected / exposed	4 / 6 (66.67%)	8 / 12 (66.67%)	5 / 6 (83.33%)
occurrences (all)	8	30	17
Nausea			
subjects affected / exposed	5 / 6 (83.33%)	9 / 12 (75.00%)	3 / 6 (50.00%)
occurrences (all)	7	10	5
Abdominal pain			
subjects affected / exposed	3 / 6 (50.00%)	1 / 12 (8.33%)	2 / 6 (33.33%)
occurrences (all)	3	1	2
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Epigastric discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lip ulceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faeces pale			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Diaphragmatic hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glossitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Haematochezia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lip blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Duodenogastric reflux			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia teeth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lip pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Liver injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Skin ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proteinuria			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	2 / 12 (16.67%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Musculoskeletal pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Liver function test abnormal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Liver abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Biliary sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Atypical pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COVID-19 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Fungal skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Labyrinthitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nipple infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	2	2
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cachexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Magnesium deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Module 1 Part A-Cohort 4 360 mg OD	Module 1 Part A-Cohort 5 180 mg BID	Module 1 Part B-1 360mg OD (TNBC)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	8 / 8 (100.00%)	23 / 23 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Breast cancer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	2	1	0
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Flushing subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	2 / 23 (8.70%) 2
Surgical and medical procedures			
Chest tube insertion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Tooth repair subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	1 / 23 (4.35%) 1
General disorders and administration site conditions			
Mucosal inflammation subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 8 (0.00%) 0	2 / 23 (8.70%) 2
Fatigue subjects affected / exposed occurrences (all)	6 / 12 (50.00%) 10	2 / 8 (25.00%) 3	11 / 23 (47.83%) 13
Crepitations subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	1 / 23 (4.35%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Biliary tract infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 8 (12.50%) 1	0 / 23 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Chills			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Disease progression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Facial pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menometrorrhagia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Breast pain			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Breast discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Nipple exudate bloody			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Priapism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	2 / 23 (8.70%)
occurrences (all)	2	1	3
Cough			
subjects affected / exposed	0 / 12 (0.00%)	3 / 8 (37.50%)	3 / 23 (13.04%)
occurrences (all)	0	3	3
Dyspnoea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	2	0	2
Pleural effusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	1	0	2
Epistaxis			

subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	1 / 23 (4.35%)
occurrences (all)	0	3	1
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
Pulmonary embolism			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Dyspnoea at rest			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Haemoptysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Disorientation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Emotional distress			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Blood creatine increased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	2	1	1
Alanine aminotransferase increased			
subjects affected / exposed	4 / 12 (33.33%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	4	1	1
Neutrophil count decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	2
White blood cell count decreased			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Weight decreased			
subjects affected / exposed	2 / 12 (16.67%)	2 / 8 (25.00%)	0 / 23 (0.00%)
occurrences (all)	2	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	1
Hyperphosphataemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Lymph node palpable			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Blood magnesium decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	2
Oxygen saturation decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1

Reticulocyte count increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	1 / 23 (4.35%) 1
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	2 / 23 (8.70%) 4
Blood urea increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	1 / 23 (4.35%) 1
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Clavicle fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 8 (12.50%) 3	0 / 23 (0.00%) 0
Multiple fractures subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Burn oral cavity subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Thermal burn subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Sunburn			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Wound complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Pericardial effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	2
Atrial fibrillation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Atrial flutter			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	3
Paraesthesia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	1	2	0
Dizziness			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	2	1	0
Intention tremor			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Nystagmus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Ageusia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Dyskinesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Electric shock sensation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lethargy			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Cluster headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Dysarthria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	2	2	1
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	5	5	4
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Visual impairment			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eye discharge			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 12 (100.00%)	6 / 8 (75.00%)	21 / 23 (91.30%)
occurrences (all)	27	13	67
Dyspepsia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	10 / 12 (83.33%)	7 / 8 (87.50%)	14 / 23 (60.87%)
occurrences (all)	15	10	32
Nausea			
subjects affected / exposed	11 / 12 (91.67%)	6 / 8 (75.00%)	22 / 23 (95.65%)
occurrences (all)	20	9	40
Abdominal pain			
subjects affected / exposed	5 / 12 (41.67%)	1 / 8 (12.50%)	6 / 23 (26.09%)
occurrences (all)	6	1	7
Constipation			
subjects affected / exposed	4 / 12 (33.33%)	0 / 8 (0.00%)	7 / 23 (30.43%)
occurrences (all)	6	0	9
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	2 / 23 (8.70%)
occurrences (all)	0	2	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 12 (8.33%)	2 / 8 (25.00%)	0 / 23 (0.00%)
occurrences (all)	2	3	0

Dry mouth			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	1	1	1
Dysphagia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Abdominal discomfort			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Mouth ulceration			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	2
Oral pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Inguinal hernia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	1	1	1

Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 8 (25.00%) 2	0 / 23 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Lip ulceration subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Faeces pale subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Retching subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	3 / 23 (13.04%) 8
Diaphragmatic hernia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Frequent bowel movements subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Gingival pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0
Glossitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 8 (0.00%) 0	0 / 23 (0.00%) 0

Haematochezia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lip blister			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Paraesthesia oral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cheilitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Proctalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Duodenogastric reflux			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia teeth			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lip pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Liver injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	0	1	2
Skin exfoliation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Dermatitis contact			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Blister			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Rash pruritic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Skin ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Skin mass			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Proteinuria			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Urinary tract obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	4
Groin pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Musculoskeletal pain			

subjects affected / exposed	1 / 12 (8.33%)	2 / 8 (25.00%)	0 / 23 (0.00%)
occurrences (all)	1	2	0
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	2 / 8 (25.00%)	1 / 23 (4.35%)
occurrences (all)	2	2	2
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Tooth infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Liver function test abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Liver abscess			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Biliary sepsis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Atypical pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
COVID-19 pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Fungal skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	2
Ear infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1

Labyrinthitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Nipple infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	1	0	1
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 12 (25.00%)	1 / 8 (12.50%)	3 / 23 (13.04%)
occurrences (all)	6	1	5
Dehydration			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cachexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Magnesium deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Module 1 Part B-2 360mg OD (CRPC)	Module 2 Part A CT7001 240 mg OD + fulvestrant (Cohort 1)	Module 2 Part A CT7001 360 mg OD + fulvestrant (Cohort 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	6 / 6 (100.00%)	25 / 25 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Tumour pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Breast cancer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)	1 / 25 (4.00%)
occurrences (all)	0	2	1
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Lymphoedema			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Flushing subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Surgical and medical procedures Chest tube insertion subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Tooth repair subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
General disorders and administration site conditions Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	2 / 25 (8.00%) 5
Fatigue subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	2 / 6 (33.33%) 4	8 / 25 (32.00%) 14
Crepitations subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 2
Biliary tract infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Asthenia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Infusion site extravasation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Injection site bruising			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Disease progression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Facial pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Menometrorrhagia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Vulvovaginal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Breast discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nipple exudate bloody			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pelvic pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Priapism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	1 / 25 (4.00%)
occurrences (all)	2	2	2
Dyspnoea			
subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	3 / 25 (12.00%)
occurrences (all)	4	2	4
Pleural effusion			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Rhinalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Dyspnoea at rest			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1

Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	3
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	3
Depressed mood			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Disorientation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Emotional distress			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	3	0	1
Blood creatine increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 11 (18.18%)	5 / 6 (83.33%)	0 / 25 (0.00%)
occurrences (all)	3	5	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	5 / 25 (20.00%)
occurrences (all)	3	4	11
Neutrophil count decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	2	3
White blood cell count decreased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	5 / 25 (20.00%)
occurrences (all)	2	0	5
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Hyperphosphataemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Lymph node palpable			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Blood magnesium decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Reticulocyte count increased subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Blood urea increased subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1
Clavicle fracture subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Multiple fractures subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Burn oral cavity subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Thermal burn subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Sunburn			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Humerus fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Atrioventricular block first degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Cardiac failure			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Atrial flutter			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0

Nervous system disorders			
Neuralgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	2	0	4
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)	1 / 25 (4.00%)
occurrences (all)	0	2	1
Headache			
subjects affected / exposed	0 / 11 (0.00%)	4 / 6 (66.67%)	4 / 25 (16.00%)
occurrences (all)	0	17	6
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	0	1	5
Intention tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nystagmus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Ageusia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Dyskinesia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Electric shock sensation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Lethargy			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Peripheral motor neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	4
Tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Cluster headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Spinal cord compression			

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	4	1	12
Lymphadenopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	4 / 11 (36.36%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	5	0	6
Leukopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	5
Lymphopenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	6
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Visual impairment			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Eye discharge			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 11 (90.91%)	5 / 6 (83.33%)	23 / 25 (92.00%)
occurrences (all)	16	14	72
Dyspepsia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	6 / 11 (54.55%)	6 / 6 (100.00%)	17 / 25 (68.00%)
occurrences (all)	9	8	49
Nausea			
subjects affected / exposed	8 / 11 (72.73%)	6 / 6 (100.00%)	19 / 25 (76.00%)
occurrences (all)	13	15	40
Abdominal pain			
subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	7 / 25 (28.00%)
occurrences (all)	2	2	10
Constipation			
subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	6 / 25 (24.00%)
occurrences (all)	2	3	8
Abdominal pain upper			
subjects affected / exposed	1 / 11 (9.09%)	2 / 6 (33.33%)	6 / 25 (24.00%)
occurrences (all)	1	2	7
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2

Dry mouth			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Dysphagia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	5
Abdominal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Abdominal pain lower			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Lip ulceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Faeces pale			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)	2 / 25 (8.00%)
occurrences (all)	0	2	2
Diaphragmatic hernia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Frequent bowel movements			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Gingival pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Glossitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	3

Haematochezia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Lip blister			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Lip dry			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Paraesthesia oral			
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Cheilitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Duodenogastric reflux			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia teeth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Lip pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Liver injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	5 / 25 (20.00%)
occurrences (all)	1	2	5
Skin exfoliation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	2
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Blister			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1

Skin ulcer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Haematuria			
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	3	0	1
Pollakiuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Proteinuria			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Urinary tract obstruction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Chronic kidney disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 6 (33.33%)	0 / 25 (0.00%)
occurrences (all)	1	3	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	4
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	2	3	8
Musculoskeletal pain			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Joint swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 11 (9.09%)	2 / 6 (33.33%)	1 / 25 (4.00%)
occurrences (all)	1	2	1
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Musculoskeletal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	2	0	3
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Tooth infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Liver abscess			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Biliary sepsis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Atypical pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
COVID-19 pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1

Fungal skin infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Vulvitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Labyrinthitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nipple infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Device related infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 11 (54.55%)	2 / 6 (33.33%)	11 / 25 (44.00%)
occurrences (all)	8	2	14
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	7
Hypocalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	4
Hypoalbuminaemia			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	3	1	6
Hypomagnesaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Cachexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Acidosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	5
Hypokalaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	5 / 25 (20.00%)
occurrences (all)	1	1	5
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	4
Hypophosphataemia			
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	3	0	2
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Magnesium deficiency			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Module 4-120 mg OD	Module 4 360 mg OD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	7 / 7 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tumour pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Breast cancer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Haematoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lymphoedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Flushing			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Surgical and medical procedures			
Chest tube insertion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tooth repair			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	6 / 8 (75.00%)	2 / 7 (28.57%)	
occurrences (all)	8	2	
Crepitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Biliary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Chills			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Infusion site extravasation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Injection site bruising			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Disease progression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Facial pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Prothrombin time prolonged			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Menometrorrhagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Breast pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Breast discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nipple exudate bloody			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pelvic pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Priapism			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	2 / 8 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Cough			
subjects affected / exposed	3 / 8 (37.50%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Epistaxis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dyspnoea exertional			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Increased viscosity of upper respiratory secretion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rhinalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dyspnoea at rest			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Haemoptysis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	3	
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Depressed mood			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Disorientation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Emotional distress			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood creatine increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
White blood cell count decreased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hyperphosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lymph node palpable			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood glucose increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Body temperature increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood magnesium decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Oxygen saturation decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Reticulocyte count increased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	
Blood urea increased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Clavicle fracture subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Contusion subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Multiple fractures subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Burn oral cavity subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Thermal burn subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Sunburn			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Humerus fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Wound complication			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rib fracture			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Sinus bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Atrioventricular block first degree			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Cardiac failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Atrial flutter			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Nervous system disorders			
Neuralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	2 / 8 (25.00%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dizziness			
subjects affected / exposed	2 / 8 (25.00%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Intention tremor			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nystagmus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Presyncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Ageusia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dyskinesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Electric shock sensation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lethargy			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Taste disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Cluster headache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dysarthria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Spinal cord compression			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lymphopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Visual impairment			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	
Vitreous floaters subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Eye discharge subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Eye pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 7 (14.29%) 1	
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	7 / 8 (87.50%) 17	6 / 7 (85.71%) 13	
Dyspepsia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 13	4 / 7 (57.14%) 9	
Nausea subjects affected / exposed occurrences (all)	7 / 8 (87.50%) 11	5 / 7 (71.43%) 15	
Abdominal pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	1 / 7 (14.29%) 1	
Constipation subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 5	2 / 7 (28.57%) 3	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 7 (0.00%) 0	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 7 (0.00%) 0	

Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Abdominal discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Mouth ulceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Oral pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Inguinal hernia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Epigastric discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gastritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Abdominal pain lower		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Abdominal distension		
subjects affected / exposed	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	1	1
Lip ulceration		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Toothache		
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	1
Faeces pale		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Retching		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Stomatitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Diaphragmatic hernia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Flatulence		
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	1	0
Frequent bowel movements		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Gingival pain		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Glossitis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0

Haematochezia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lip blister			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lip dry			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Paraesthesia oral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Cheilitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Proctalgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Duodenogastric reflux			
subjects affected / exposed	2 / 8 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dental caries			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Hyperaesthesia teeth			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypoaesthesia oral			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Lip pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypertransaminasaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Liver injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Skin exfoliation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	1 / 8 (12.50%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Dermatitis contact			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blister			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Rash pruritic			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

Skin ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin mass			
subjects affected / exposed	2 / 8 (25.00%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Rash erythematous			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Acute kidney injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dysuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Proteinuria			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Urinary tract obstruction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Chronic kidney disease			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Glycosuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Groin pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Bone pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal pain			

subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pain in jaw			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Fungal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Tooth infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 8 (25.00%)	1 / 7 (14.29%)	
occurrences (all)	2	2	
Liver function test abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Liver abscess			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Biliary sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Wound infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Atypical pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Candida infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Fungal skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Laryngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vulvitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gingivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Ear infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Labyrinthitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nipple infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hordeolum			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Device related infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 8 (37.50%)	2 / 7 (28.57%)	
occurrences (all)	4	2	
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Hypoalbuminaemia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Hyperglycaemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Hypomagnesaemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Cachexia		
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)
occurrences (all)	1	0
Acidosis		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Gout		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Hypercalcaemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Hypokalaemia		
subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	1
Hyponatraemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Hypophosphataemia		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Diabetes mellitus inadequate control		
subjects affected / exposed	0 / 8 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0
Magnesium deficiency		
subjects affected / exposed	1 / 8 (12.50%)	1 / 7 (14.29%)
occurrences (all)	1	1
Diabetes mellitus		

subjects affected / exposed	0 / 8 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 7 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2017	Protocol Amendment Version 2.0, reason for amendment: <ul style="list-style-type: none">• Further guidance on the MTD added• New exclusion criteria added to exclude patients who had received a live virus vaccination within 28 days of study entry• Additional rationale for the starting dose added and clarification added on the dose escalation scheme• Requirement for a pregnancy test changed from every other cycle to every cycle
28 March 2018	Protocol amendment Version 4.0, reason for amendment- <ul style="list-style-type: none">• Clarified that if an increase in the daily dose was made this would not exceed the maximum total daily dose that had been explored and was tolerable• Requirement for a minimum of 7 days between completion of dosing in the first 21-day cycle in one cohort to the start of dosing in the subsequent cohort removed.• Clarification add as to what changes could be implemented following safety data review and agreement by the SRC, without the requirement to submit a substantial amendment to the IEC or the Regulatory Authorities. The frequency of PK sampling could also be modified based on SRC review and may include up to 3 additional PK samples of 4 mL each within any given cycle, to better characterize the individual PK profile based upon emerging PK data. <p>Additionally, the following changes made in Version 3.0 (the protocol not implemented) were included in the Version 4.0:</p> <ul style="list-style-type: none">• Clarification of what changes could be implemented following review of the safety data by the SRC without the requirement to submit a substantial amendment• Clarification that the SRC could remove the requirement for participants to be dosed in a fasted state based on emerging pre-clinical and clinical data• Removal of the 7-day staggering interval for the second participant dosed in a cohort• PK sampling period extended to up to 168 hours and related changes to blood volumes collected• Exclusion criteria relating to prior receipt of a CDK inhibitor removed.
10 July 2018	Protocol amendment Version 5.0, reason for amendment- <p>Updated details added on Module 4 to evaluate effect of food on the PK of CT7001 when given as monotherapy to participants with advanced solid malignancies (fed and fasting study).</p>
25 September 2018	Protocol Amendment Version 6.0, reason for amendment <ul style="list-style-type: none">• The protocol was separated out into a core protocol (Volume 1 and separate modules (Volumes 2 to 7)• Details added on Module 1B-1 (TNBC cohort)• All sections of the core protocol, including the introduction and background, were re-structured in the core protocol and updated to make it consistent with Module 1B-1 (TNBC).

06 March 2019	<p>Protocol amendment Version 8.0, reason for amendment-</p> <ul style="list-style-type: none"> •Wording for dose escalation in Module 2 updated to provide clarification that dose escalation must be stopped and a new substantial amendment approved if a lower dose or different dosing regimen was employed. •The Lead Biostatistician details were updated in the protocol approval signature page, along with updates to the Medical Monitor details and SAE reporting requirements. <p>Note: Version 7.0 was not implemented ; Module 2 was removed from the main protocol and added as a separate module.</p>
26 March 2019	<p>Protocol amendment Version 9.0, reason for amendment-</p> <ul style="list-style-type: none"> •Details added on Module 1B-2 (CRPC cohort) •Module 2 split into Parts A and B and details added on Part C •Introduction and background in the core protocol updated •MTD and preliminary recommended Phase 2 dose details updated •Contraception requirements updated to clarify contra-indication of some hormonal contraceptives in certain populations •Prohibited medications updated to permit participants with prostate cancer or pre/perimenopausal breast cancer to receive goserelin •Current PK/ PD, clinical and safety data updated as of 26 Nov 2018 and efficacy data updated as of per 24 Sep 2018.
30 January 2020	<p>Protocol amendment Version 11.0, reason for amendment</p> <ul style="list-style-type: none"> •Medical Monitor details changed to Pharmaceutical Product Development, LLC for Module 2 •Interactive web response system (IWRS) added to allocate CT7001 medication bottles to the participants •Requirement to interrupt or delay treatment due to Grade ≥ 4 thrombocytopenia changed to Grade ≥ 3 and platelet count level needed to restart treatment increased •Definition of an AESI added to the protocol, along with requirements for reporting AESIs •Overall risk/benefit assessment updated based on available non-clinical and clinical safety data as of 07 Jan 2020. <p>The changes made in Version 10.0 (protocol not implemented) were also included in Version 11.0</p> <ul style="list-style-type: none"> •Introduction and background in the core protocol updated with latest PK/PD, clinical, efficacy data and modular status as per 10 Sep 2019 •Coagulation parameters removed from core laboratory tests •Timings of some exclusion criteria clarified •Fasting requirement for dosing removed as per SRC conclusion that food had no clinically relevant effect on the bioavailability of CT7001 •MTD and recommended Phase 2 dose of 360 mg OD taken forward to Module 4 Cohort 2, M1B-1 (TNBC and CRPC cohorts), and was also the target dose in Module 2. <ul style="list-style-type: none"> •Threshold for delayed dosing due to thrombocytopenia updated and level for dosing restart increased •Reference to goserelin removed and replaced with 'LHRH agonist or, where applicable, surgical castration' •Cannabinoids/cannabis oil added to the medications not recommended •Hair samples were added to the core biomarker analysis section and information for collection blood for CTCs and assessment of CYP and drug transporter genes added in section exploratory research.
27 April 2020	<p>Protocol amendment Version 12.0, reason for amendment-</p> <p>The number of participants included in Module 1B-1 was increased to 30.</p>

15 July 2020	<p>Protocol amendment Version 13.0, reason for amendment</p> <ul style="list-style-type: none"> •References to Module 1A solid tumor cohort have been deleted since this module was no longer being conducted •Introduction and background updated with latest clinical and efficacy data, as of 01 Jun 2020 •IWRS changed to IXRS •Exclusion criteria numbers 12 and 15 updated to clarify receipt of cytotoxic and small molecule IMP within 28 days or ≤ 5 half-lives, whichever is shorter, before the first dose of IMP •Anti-emetic guidance updated •IMP dose reduction, dose interruption or delay updated for Grade ≥ 3 anemia and treatment resumption on 240 mg OD after Grade ≥ 3 thrombocytopenia (platelet count $< 50 \times 10^9/L$) added •New section added outlining the concurrent and palliative radiotherapy or surgeries that were permitted during the active treatment phase of the study •HbA1c added to the laboratory safety assessments and the requirement for a fasted glucose test added for participants with a medical history of diabetes <ul style="list-style-type: none"> •Requirement for blood samples for PBMCs to be used for Nanostring analyses removed from Module 1 Part B •Reference to collection of hair samples for biomarker analysis deleted •A new appendix was added to detail the sponsors actions and responses to the COVID-19 pandemic.
23 December 2020	<p>Protocol Amendment Version 14.0, reason for amendment-</p> <ul style="list-style-type: none"> •The international non-proprietary name of samuraciclib added •Details of Module 6 added and the MTD and recommended Phase 2 dose of 360 mg OD added throughout the module •Introduction and background updated with latest data as of 16 Nov 2020 •Permitted and/or recommended treatment provision of anti- emetic medication that should be given prophylactically for nausea and/or vomiting as indicated by the investigator and in accordance with the current DMC guidelines v1.0 dated 26 Oct 2020 •Nausea and vomiting guidelines added as an appendix
14 June 2021	<p>Protocol amendment Version 15.0, reason for amendment</p> <ul style="list-style-type: none"> • Introduction and background updated with latest clinical, safety and efficacy data as of 12 Apr 2021 • Definition of women not of child-bearing potential updated in inclusion criterion number 6 • Definition of a live virus updated • Changes made to permitted and recommended concomitant medications in the management of nausea, vomiting, and diarrhea. • Clarification and updates to live viruses and bacterial vaccines in prohibited medication • End of trial definition amended • Guidelines on the management of nausea, vomiting, and diarrhea updated to v2.0 dated 08 Jun 2021 • 360 mg OD confirmed as the starting dose for use in combination with fulvestrant in Module 2B.

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/37488191>