Clinical trial results:
A Phase 2 Study of ZEN003694 in Combination with Talazoparib in Patients with Triple-Negative Breast Cancer

Summary

EudraCT number	2018-003906-26
Trial protocol	BE ES
Global end of trial date	21 June 2024

Results information

Result version number	v1 (current)
This version publication date	29 May 2026
First version publication date	29 May 2026
Summary attachment (see zip file)	ZEN003694-004 Protocol for EudraCT (ZEN003694-004 Protocol for EudraCT.pdf) ZEN003694-004_CSR Report_Synopsis_EudraCT_15Mar2024 (ZEN003694-004_CSR Report_Synopsis_EudraCT_15Mar2024.pdf)

Trial information

Trial identification

Sponsor protocol code	ZEN003694-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03901469
WHO universal trial number (UTN)	-
Other trial identifiers	IND (China -for Expansion phase only): JXHL2000118, IND (China -for Expansion phase only): JXHL2000119, IND (USA): 141108

Notes:

Sponsors

Sponsor organisation name	Zenith Epigenetics Ltd.
Sponsor organisation address	300, 4820 Richard Road SW , Calgary, Alberta T3E 6L1 , Canada,
Public contact	Clinical Trial Information, Zenith Epigenetics Ltd., 1 587390-7865, ZEN003694-004@zenithepigenetics.com
Scientific contact	Clinical Trial Information, Zenith Epigenetics Ltd., 1 587390-7865, ZEN003694-004@zenithepigenetics.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	08 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2024
Global end of trial reached?	Yes
Global end of trial date	21 June 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part 1: To determine the safety, tolerability, maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of ZEN003694 in combination with talazoparib in patients with locally advanced or metastatic triple-negative breast cancer (TNBC)
Part 2: To evaluate the efficacy of ZEN003694 in combination with talazoparib in patients with locally advanced or metastatic TNBC
Expansion: To evaluate the efficacy of ZEN003694 in combination with talazoparib in patients with locally advanced or metastatic TNBC whose cancer was hormone receptor negative (<5%) at the time of initial breast cancer diagnosis and who have received TROP2-ADC therapy in the unresectable locally advanced or metastatic disease setting.

Protection of trial subjects:

Managed through Institutional Review Boards, informed patient consent and data confidentiality protocols, as well as routine monitoring of clinical sites.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	United States: 42
Country: Number of subjects enrolled	China: 32
Worldwide total number of subjects	115
EEA total number of subjects	41

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	93
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at nineteen investigational sites in the United States (eight), Belgium (two), Spain (two), and China (seven) between June 2019 and March 2024.

Pre-assignment

Screening details:

Participants ≥ 18 years with metastatic or recurrent or locally advanced TNBC without germline mutations in BRCA1 or BRCA2.

Period 1

Period 1 title	Between June 2019 and March 2024 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Part 1 Dose Escalation Cohort 1

Arm description:

ZEN003694 48 mg PO QD with Talazoparib 1 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

48 mg ZEN003694 PO QD

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

Dosage and administration details:

1 mg Talazoparib PO QD

Arm title	Part 1 Dose Escalation Cohort 2

Arm description:

ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

48 mg ZEN003694 PO QD

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

Dosage and administration details:

0.75 mg Talazoparib PO QD

Arm title	Part 1 Dose Escalation Cohort 3

Arm description:

ZEN003694 36 mg PO QD with Talazoparib 1 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

36 mg ZEN003694 PO QD

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

Dosage and administration details:

1 mg Talazoparib PO QD

Arm title	Part 2 Stages 1 and 2

Arm description:

ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

48 mg ZEN003694 PO QD

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

Dosage and administration details:

0.75 mg Talazoparib PO QD

Arm title	Expansion Cohort A

Arm description:

Combination Treatment in Post-TROP2-ADC Patients. ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

48 mg ZEN003694 PO QD

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

Dosage and administration details:

0.75 mg Talazoparib PO QD

Arm title	Expansion Cohort B - ZEN003694 Monotherapy

Arm description:

ZEN003694 48 mg PO QD as monotherapy at the in 28-day cycles with the option to cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

48 mg ZEN003694 PO QD

Arm title	Expansion Cohort C

Arm description:

Combination Treatment in TROP2-ADC-naïve patients. ZEN003694 48 mg PO QD with Talazoparib PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in China only.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

48 mg ZEN003694 PO QD

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

Dosage and administration details:

0.75 mg Talazoparib PO QD

Arm title	Expansion Cohort B - Cross-over Combination

Arm description:

Post cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Arm type	Experimental
Investigational medicinal product name	ZEN003694
Investigational medicinal product code	
Other name	ZEN-3694
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

48 mg ZEN003694 PO QD

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

Dosage and administration details:

0.75 mg Talazoparib PO QD

Number of subjects in period 1	Part 1 Dose Escalation Cohort 1	Part 1 Dose Escalation Cohort 2	Part 1 Dose Escalation Cohort 3
Started	6	8	3
Completed	0	0	0
Not completed	6	8	3
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	1	-	-
Death	-	-	-
Termination of study by sponsor	-	-	-
not disclosed	1	-	-
Withdrawal by Physician	-	-	-
Clinical Progression	-	2	-
Radiographic Progression	4	6	3

Number of subjects in period 1	Part 2 Stages 1 and 2	Expansion Cohort A	Expansion Cohort B - ZEN003694 Monotherapy
Started	42	21	3
Completed	0	0	0
Not completed	42	21	3
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	-	-	-
Death	3	5	-
Termination of study by sponsor	-	1	1
not disclosed	1	-	-

Withdrawal by Physician	1	-	-
Clinical Progression	7	6	-
Radiographic Progression	30	7	2

Number of subjects in period 1	Expansion Cohort C	Expansion Cohort B - Cross-over Combination
Started	32	1
Completed	0	0
Not completed	32	1
Consent withdrawn by subject	8	-
Adverse event, non-fatal	9	-
Death	1	-
Termination of study by sponsor	-	-
not disclosed	1	-
Withdrawal by Physician	-	-
Clinical Progression	2	-
Radiographic Progression	11	1

Baseline characteristics

Reporting groups	
Reporting group title	Part 1 Dose Escalation Cohort 1
Reporting group description:	
ZEN003694 48 mg PO QD with Talazoparib 1 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Part 1 Dose Escalation Cohort 2
Reporting group description:	
ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Part 1 Dose Escalation Cohort 3
Reporting group description:	
ZEN003694 36 mg PO QD with Talazoparib 1 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Part 2 Stages 1 and 2
Reporting group description:	
ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Expansion Cohort A
Reporting group description:	
Combination Treatment in Post-TROP2-ADC Patients. ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Expansion Cohort B - ZEN003694 Monotherapy
Reporting group description:	
ZEN003694 48 mg PO QD as monotherapy at the in 28-day cycles with the option to cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Expansion Cohort C
Reporting group description:	
Combination Treatment in TROP2-ADC-naïve patients. ZEN003694 48 mg PO QD with Talazoparib PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in China only.	
Reporting group title	Expansion Cohort B - Cross-over Combination
Reporting group description:	
Post cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	

Reporting group values	Part 1 Dose Escalation Cohort 1	Part 1 Dose Escalation Cohort 2	Part 1 Dose Escalation Cohort 3
Number of subjects	6	8	3
Age categorical Units: Subjects			
Adults (18-64 years)	4	7	3
From 65-84 years	2	1	0

Age continuous			
Units: years			
arithmetic mean	57.2	52.8	59.3
standard deviation	± 14.8	± 11.7	± 4.0
Gender categorical			
Female subjects have been enrolled in the study.			
Units: Subjects			
Female	6	8	3

Reporting group values	Part 2 Stages 1 and 2	Expansion Cohort A	Expansion Cohort B - ZEN003694 Monotherapy
Number of subjects	42	21	3
Age categorical			
Units: Subjects			
Adults (18-64 years)	33	19	2
From 65-84 years	9	2	1
Age continuous			
Units: years			
arithmetic mean	52.2	49.2	55.3
standard deviation	± 12.1	± 11.7	± 10.1
Gender categorical			
Female subjects have been enrolled in the study.			
Units: Subjects			
Female	42	21	3

Reporting group values	Expansion Cohort C	Expansion Cohort B - Cross-over Combination	Total
Number of subjects	32	1	115
Age categorical			
Units: Subjects			
Adults (18-64 years)	25	1	93
From 65-84 years	7	0	22
Age continuous			
Units: years			
arithmetic mean	54.9	49	
standard deviation	± 10.7	± 0	-
Gender categorical			
Female subjects have been enrolled in the study.			
Units: Subjects			
Female	32	1	115

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All participants were included in the full analysis set

Reporting group values	Full Analysis Set		
Number of subjects	115		
Age categorical Units: Subjects			
Adults (18-64 years)	93		
From 65-84 years	22		
Age continuous Units: years			
arithmetic mean	53.0		
standard deviation	± 11.6		
Gender categorical			
Female subjects have been enrolled in the study.			
Units: Subjects			
Female	115		

End points

End points reporting groups

Reporting group title	Part 1 Dose Escalation Cohort 1
Reporting group description:	
ZEN003694 48 mg PO QD with Talazoparib 1 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Part 1 Dose Escalation Cohort 2
Reporting group description:	
ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Part 1 Dose Escalation Cohort 3
Reporting group description:	
ZEN003694 36 mg PO QD with Talazoparib 1 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Part 2 Stages 1 and 2
Reporting group description:	
ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Expansion Cohort A
Reporting group description:	
Combination Treatment in Post-TROP2-ADC Patients. ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Expansion Cohort B - ZEN003694 Monotherapy
Reporting group description:	
ZEN003694 48 mg PO QD as monotherapy at the in 28-day cycles with the option to cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Reporting group title	Expansion Cohort C
Reporting group description:	
Combination Treatment in TROP2-ADC-naïve patients. ZEN003694 48 mg PO QD with Talazoparib PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in China only.	
Reporting group title	Expansion Cohort B - Cross-over Combination
Reporting group description:	
Post cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants were included in the full analysis set	

Primary: Part 1: Number of Participants With Dose-limiting Toxicities (DLT)

End point title	Part 1: Number of Participants With Dose-limiting Toxicities (DLT)[1][2]
End point description:	
Determination of DLT will be made during the first 28 days of treatment (i.e., Cycle 1) in the dose	

escalation phase. A DLT is defined as a clinically significant AE or laboratory abnormality that is considered possibly, probably or definitely related to study drug.

End point type	Primary

End point timeframe:

Cycle 1, Up to 1 month

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: Trial was terminated, no statistical analysis performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Trial was terminated, no statistical analysis performed.

End point values	Part 1 Dose Escalation Cohort 1	Part 1 Dose Escalation Cohort 2	Part 1 Dose Escalation Cohort 3	Full Analysis Set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	8	3	17
Units: Number of Participants with DLT	2	1	0	2

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Treatment-related Adverse Events (AE)

End point title	Incidence of Treatment-related Adverse Events (AE)[3][4]

End point description:

Adverse events were collected in all participants. For an event to be recorded as an AE, the onset must occur during or after the patient's first exposure to study drug and no later than 30 days after the last study drug dose.

End point type	Primary

End point timeframe:

Cycle 1 Day 1 to 30 days post last dose (each cycle is 28 days) up to 22 months

Notes:

[3] - 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: Trial was terminated, no statistical analysis performed.

[4] - 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: Trial was terminated, no statistical analysis performed.

End point values	Part 1 Dose Escalation Cohort 1	Part 1 Dose Escalation Cohort 2	Part 1 Dose Escalation Cohort 3	Part 2 Stages 1 and 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	8	3	42
Units: Count of Participants				
Treatment Related Adverse Events	6	8	3	41
Treatment Related Serious Adverse Events	2	1	0	4

End point values	Expansion Cohort A	Expansion Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	32		
Units: Count of Participants				
Treatment Related Adverse Events	19	32		
Treatment Related Serious Adverse Events	1	13		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Benefit Rate (CBR)

End point title	Clinical Benefit Rate (CBR)[5][6]

End point description:

Percentage of patients with a best overall response of confirmed complete response (CR), partial response (PR), or stable disease (SD ≥ 4 cycles) by RECIST v1.1. Parts 1 and 2, Expansion Cohorts A and C. Patients who have received at least 3 weeks of per-protocol treatment during Cycle 1, or <3 weeks of treatment in Cycle 1 because of a DLT, will comprise the Efficacy Population. Patients who were determined to be "unevaluable" during Cycle 1 by the Sponsor and Investigator will not be included in the Efficacy Population.

End point type	Primary

End point timeframe:

From screening up to 18 months

Notes:

[5] - 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: Trial was terminated, no statistical analysis performed.

[6] - 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: Trial was terminated, no statistical analysis performed.

End point values	Part 1 Dose Escalation Cohort 1	Part 1 Dose Escalation Cohort 2	Part 1 Dose Escalation Cohort 3	Part 2 Stages 1 and 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	3	37
Units: % of Participants				
number (not applicable)	33.3	66.7	33.3	32.4

End point values	Expansion Cohort A	Expansion Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: % of Participants				
number (not applicable)	0	11.1		

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[7][8]

End point description:

Percentage of participants with a confirmed complete response (CR) or partial response (PR) by RECIST 1.1.

End point type	Primary

End point timeframe:

From screening up to 18 months

Notes:

[7] - 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: Trial was terminated, no statistical analysis performed.

[8] - 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: Trial was terminated, no statistical analysis performed.

End point values	Part 1 Dose Escalation Cohort 1	Part 1 Dose Escalation Cohort 2	Part 1 Dose Escalation Cohort 3	Part 2 Stages 1 and 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	3	37
Units: %				
number (not applicable)	33.3	16.7	33.3	21.6

End point values	Expansion Cohort A	Expansion Cohort C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: %				
number (not applicable)	0	5.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Cycle 1 Day 1 to 30 days post last dose (each cycle is 28 days) up to 22 months.

Adverse event reporting additional description:

Adverse events were collected in all participants. For an event to be recorded as an AE, the onset must occur during or after the patient's first exposure to study drug and no later than 30 days after the last study drug .

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Part 1 Dose Escalation: Cohort 1

Reporting group description:

ZEN003694 48 mg PO QD with Talazoparib 1 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Reporting group title	Part 1 Dose Escalation: Cohort 2

Reporting group description:

ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Reporting group title	Part 1 Dose Escalation: Cohort 3

Reporting group description:

ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Reporting group title	Part 2 Stages 1 and 2

Reporting group description:

ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Reporting group title	Expansion Cohort A

Reporting group description:

Combination Treatment in Post-TROP2-ADC Patients. ZEN003694 48 mg PO QD with Talazoparib 0.75 mg PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2.

Reporting group title	Expansion Cohort B - Monotherapy

Reporting group description:

ZEN003694 48 mg PO QD as monotherapy at the in 28-day cycles with the option to cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Reporting group title	Expansion Cohort B - Cross-over Combination

Reporting group description:

Post cross-over to combination treatment of ZEN003694 48 mg PO QD with 0.75 mg Talazoparib PO QD at the time of disease progression (but no sooner than after 6 weeks of monotherapy). Patients have histologically confirmed Triple Negative Breast Cancer and have no documented germline mutations of BRCA1 or BRCA2. Includes sites in the US and EU.

Reporting group title	Expansion Cohort C

Reporting group description:

Combination Treatment in TROP2-ADC-naïve Patients. ZEN003694 48 mg PO QD with Talazoparib PO QD (RP2D) in 28-day cycles. Patients have histologically confirmed Triple Negative Breast Cancer and

Serious adverse events	Part 1 Dose Escalation: Cohort 1	Part 1 Dose Escalation: Cohort 2	Part 1 Dose Escalation: Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	2 / 8 (25.00%)	1 / 3 (33.33%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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			
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 3 (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

Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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			
Apraxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (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
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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 / 8 (0.00%)	0 / 3 (0.00%)
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	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
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 / 6 (0.00%)	1 / 8 (12.50%)	0 / 3 (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
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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			
Hepatic failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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			
Urinary retention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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			
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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			
Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (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
Urosepsis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
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			
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 Stages 1 and 2	Expansion Cohort A	Expansion Cohort B - Monotherapy
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 42 (26.19%)	10 / 21 (47.62%)	0 / 3 (0.00%)
number of deaths (all causes)	5	2	0
number of deaths resulting from adverse events	3	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastasis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (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
Fatigue			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	1 / 42 (2.38%)	1 / 21 (4.76%)	0 / 3 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			

subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
Dyspnoea			
subjects affected / exposed	3 / 42 (7.14%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 42 (2.38%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
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	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
White blood cell count decreased			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Cardiac failure			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sinus node dysfunction			
subjects affected / exposed	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (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			
Apraxia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
Ataxia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 21 (4.76%)	0 / 3 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
Spinal cord compression			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			

subjects affected / exposed	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (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
Syncope			
subjects affected / exposed	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	3 / 42 (7.14%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
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 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
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	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
Hypertransaminasaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (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
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
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			
Muscular weakness			
subjects affected / exposed	0 / 42 (0.00%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (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
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 21 (0.00%)	0 / 3 (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

Serious adverse events	Expansion Cohort B - Cross-over Combination	Expansion Cohort C	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	14 / 32 (43.75%)	
number of deaths (all causes)	0	5	
number of deaths resulting from adverse events	0	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastasis			

subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm progression			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 1 (0.00%)	2 / 32 (6.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	

Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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			
Atelectasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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 / 1 (0.00%)	0 / 32 (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 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	7 / 32 (21.88%)	
occurrences causally related to treatment / all	0 / 0	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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			
Apraxia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			

subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			

subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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 / 1 (0.00%)	0 / 32 (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 / 1 (0.00%)	2 / 32 (6.25%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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			
Urinary retention			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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			
Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (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: 0.05 %

Non-serious adverse events	Part 1 Dose Escalation: Cohort 1	Part 1 Dose Escalation: Cohort 2	Part 1 Dose Escalation: Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	8 / 8 (100.00%)	3 / 3 (100.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 8 (37.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	3 / 8 (37.50%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Blood creatinine increased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Neutrophil count decreased			

subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Platelet count decreased			
subjects affected / exposed	3 / 6 (50.00%)	4 / 8 (50.00%)	0 / 3 (0.00%)
occurrences (all)	3	4	0
Weight decreased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
White blood cell count decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	2 / 3 (66.67%)
occurrences (all)	2	1	2
Thrombocytopenia			
subjects affected / exposed	3 / 6 (50.00%)	1 / 8 (12.50%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	1 / 3 (33.33%)
occurrences (all)	1	1	1

Fatigue			
subjects affected / exposed	4 / 6 (66.67%)	3 / 8 (37.50%)	1 / 3 (33.33%)
occurrences (all)	4	3	1
Malaise			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Dyschromatopsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Photopsia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	3 / 8 (37.50%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Diarrhoea			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Dry mouth			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dysphagia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	3 / 6 (50.00%)	5 / 8 (62.50%)	0 / 3 (0.00%)
occurrences (all)	3	5	0
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	4 / 8 (50.00%)	0 / 3 (0.00%)
occurrences (all)	2	4	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Dyspnoea			
subjects affected / exposed	3 / 6 (50.00%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Back pain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 6 (50.00%)	3 / 8 (37.50%)	1 / 3 (33.33%)
occurrences (all)	3	3	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hypermagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2 Stages 1 and 2	Expansion Cohort A	Expansion Cohort B - Monotherapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)	21 / 21 (100.00%)	2 / 3 (66.67%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	10 / 42 (23.81%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	10	3	0
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 42 (28.57%)	5 / 21 (23.81%)	0 / 3 (0.00%)
occurrences (all)	12	5	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 42 (4.76%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Blood bilirubin increased			
subjects affected / exposed	2 / 42 (4.76%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Blood creatinine increased			
subjects affected / exposed	5 / 42 (11.90%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	5	1	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	2 / 42 (4.76%)	4 / 21 (19.05%)	0 / 3 (0.00%)
occurrences (all)	2	4	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 42 (4.76%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			
subjects affected / exposed	6 / 42 (14.29%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	6	3	0
Neutrophil count decreased			
subjects affected / exposed	4 / 42 (9.52%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Platelet count decreased			
subjects affected / exposed	16 / 42 (38.10%)	8 / 21 (38.10%)	1 / 3 (33.33%)
occurrences (all)	16	8	1
Weight decreased			
subjects affected / exposed	2 / 42 (4.76%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
White blood cell count decreased			
subjects affected / exposed	3 / 42 (7.14%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 42 (9.52%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Dysgeusia			
subjects affected / exposed	9 / 42 (21.43%)	5 / 21 (23.81%)	0 / 3 (0.00%)
occurrences (all)	9	5	0
Headache			
subjects affected / exposed	5 / 42 (11.90%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	5	3	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	8 / 42 (19.05%)	10 / 21 (47.62%)	0 / 3 (0.00%)
occurrences (all)	8	10	0
Thrombocytopenia			
subjects affected / exposed	8 / 42 (19.05%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 42 (9.52%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Fatigue			
subjects affected / exposed	14 / 42 (33.33%)	13 / 21 (61.90%)	0 / 3 (0.00%)
occurrences (all)	14	13	0
Malaise			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	4 / 42 (9.52%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Pyrexia			
subjects affected / exposed	2 / 42 (4.76%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Dyschromatopsia			
subjects affected / exposed	4 / 42 (9.52%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Photophobia			
subjects affected / exposed	3 / 42 (7.14%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Photopsia			
subjects affected / exposed	9 / 42 (21.43%)	3 / 21 (14.29%)	1 / 3 (33.33%)
occurrences (all)	9	3	1
Vision blurred			
subjects affected / exposed	4 / 42 (9.52%)	5 / 21 (23.81%)	0 / 3 (0.00%)
occurrences (all)	4	5	0
Visual impairment			

subjects affected / exposed	6 / 42 (14.29%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	6	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 42 (9.52%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Constipation			
subjects affected / exposed	6 / 42 (14.29%)	5 / 21 (23.81%)	0 / 3 (0.00%)
occurrences (all)	6	5	0
Diarrhoea			
subjects affected / exposed	6 / 42 (14.29%)	2 / 21 (9.52%)	1 / 3 (33.33%)
occurrences (all)	6	2	1
Dry mouth			
subjects affected / exposed	2 / 42 (4.76%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Dysphagia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	19 / 42 (45.24%)	11 / 21 (52.38%)	0 / 3 (0.00%)
occurrences (all)	19	11	0
Vomiting			
subjects affected / exposed	11 / 42 (26.19%)	4 / 21 (19.05%)	1 / 3 (33.33%)
occurrences (all)	11	4	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 42 (2.38%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Dyspnoea			
subjects affected / exposed	5 / 42 (11.90%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	5	3	0
Pleural effusion			
subjects affected / exposed	2 / 42 (4.76%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			

Anxiety			
subjects affected / exposed	3 / 42 (7.14%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Insomnia			
subjects affected / exposed	2 / 42 (4.76%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 42 (9.52%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Back pain			
subjects affected / exposed	5 / 42 (11.90%)	5 / 21 (23.81%)	0 / 3 (0.00%)
occurrences (all)	5	5	0
Pain in extremity			
subjects affected / exposed	3 / 42 (7.14%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 42 (2.38%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 42 (26.19%)	7 / 21 (33.33%)	0 / 3 (0.00%)
occurrences (all)	11	7	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	6 / 42 (14.29%)	8 / 21 (38.10%)	0 / 3 (0.00%)
occurrences (all)	6	8	0
Hyperkalaemia			
subjects affected / exposed	2 / 42 (4.76%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Hypermagnesaemia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 21 (4.76%)	0 / 3 (0.00%)
occurrences (all)	1	1	0

Hyperphosphataemia			
subjects affected / exposed	2 / 42 (4.76%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 42 (2.38%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Hypocalcaemia			
subjects affected / exposed	1 / 42 (2.38%)	4 / 21 (19.05%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Hypochloraemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 21 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	2 / 42 (4.76%)	3 / 21 (14.29%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Hyponatraemia			
subjects affected / exposed	2 / 42 (4.76%)	5 / 21 (23.81%)	0 / 3 (0.00%)
occurrences (all)	2	5	0
Hypophosphataemia			
subjects affected / exposed	3 / 42 (7.14%)	2 / 21 (9.52%)	0 / 3 (0.00%)
occurrences (all)	3	2	0

Non-serious adverse events	Expansion Cohort B - Cross-over Combination	Expansion Cohort C	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	32 / 32 (100.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	13 / 32 (40.63%)	
occurrences (all)	0	13	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	13 / 32 (40.63%)	
occurrences (all)	0	13	
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Blood bilirubin increased			
subjects affected / exposed	0 / 1 (0.00%)	25 / 32 (78.13%)	
occurrences (all)	0	25	
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	8 / 32 (25.00%)	
occurrences (all)	0	8	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 1 (0.00%)	5 / 32 (15.63%)	
occurrences (all)	0	5	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	6 / 32 (18.75%)	
occurrences (all)	0	6	
Lymphocyte count decreased			
subjects affected / exposed	0 / 1 (0.00%)	8 / 32 (25.00%)	
occurrences (all)	0	8	
Neutrophil count decreased			
subjects affected / exposed	1 / 1 (100.00%)	12 / 32 (37.50%)	
occurrences (all)	1	12	
Platelet count decreased			
subjects affected / exposed	1 / 1 (100.00%)	16 / 32 (50.00%)	
occurrences (all)	1	16	
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	6 / 32 (18.75%)	
occurrences (all)	0	6	
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	12 / 32 (37.50%)	
occurrences (all)	0	12	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 1 (0.00%)	4 / 32 (12.50%)	
occurrences (all)	0	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	16 / 32 (50.00%)	
occurrences (all)	0	16	
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	7 / 32 (21.88%)	
occurrences (all)	0	7	
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	6 / 32 (18.75%)	
occurrences (all)	0	6	
Pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Eye disorders			
Dyschromatopsia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	

Photophobia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Photopsia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Vision blurred			
subjects affected / exposed	0 / 1 (0.00%)	7 / 32 (21.88%)	
occurrences (all)	0	7	
Visual impairment			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	6 / 32 (18.75%)	
occurrences (all)	0	6	
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	5 / 32 (15.63%)	
occurrences (all)	0	5	
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	19 / 32 (59.38%)	
occurrences (all)	0	19	
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	13 / 32 (40.63%)	
occurrences (all)	0	13	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 1 (0.00%)	5 / 32 (15.63%)	
occurrences (all)	0	5	
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	18 / 32 (56.25%)	
occurrences (all)	0	18	
Hypercholesterolaemia			

subjects affected / exposed	0 / 1 (0.00%)	5 / 32 (15.63%)	
occurrences (all)	0	5	
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	19 / 32 (59.38%)	
occurrences (all)	0	19	
Hyperkalaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Hypermagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 32 (12.50%)	
occurrences (all)	0	4	
Hyperphosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	2	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 1 (0.00%)	6 / 32 (18.75%)	
occurrences (all)	0	6	
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 32 (9.38%)	
occurrences (all)	0	3	
Hypochloraemia			
subjects affected / exposed	0 / 1 (0.00%)	7 / 32 (21.88%)	
occurrences (all)	0	7	
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	10 / 32 (31.25%)	
occurrences (all)	0	10	
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	12 / 32 (37.50%)	
occurrences (all)	0	12	
Hypophosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 32 (12.50%)	
occurrences (all)	0	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2019	Amendment 1: 18-March-2019 Updated ZEN003694 starting dose from 72mg to 48mg QD
29 April 2019	Amendment 2: 29-April-2019 Updated eligibility criteria
17 December 2019	Amendment 3: 17-December 2019 Update to eligibility criteria and DLT definition
11 May 2020	Amendment 4: 11-May-2020 Update to eligibility criteria and study assessments
23 February 2022	Amendment 5: 23-February-2022 Expand the study to up to 120 subjects
26 May 2022	Amendment 6: 26-May-2022 Update to eligibility criteria and study assessments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported